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Breaking Report

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Synthesis of 3-Methylthio-benzo[*b*]furans/Thiophenes via Intramolecular Cyclization of 2-Alkynylanisoles/Sulfides Mediated by DMSO/DMSO-d_6 and $SOCl_2$

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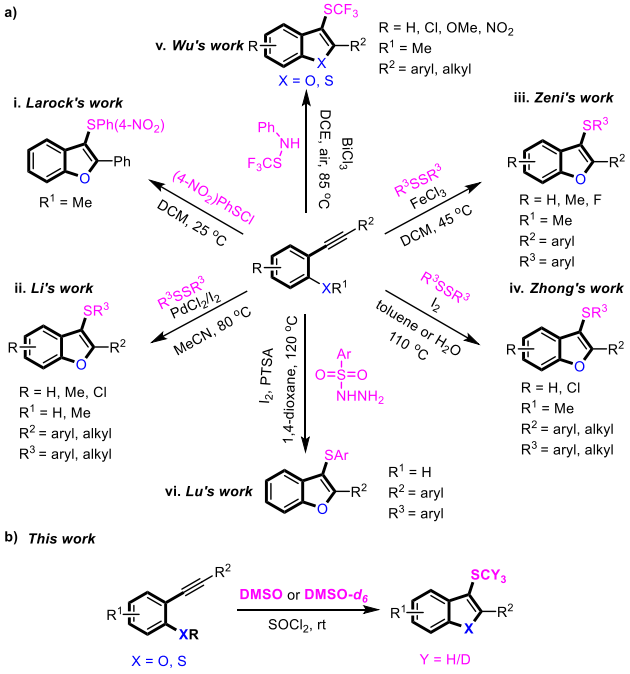
Summary of main observation and conclusion The reaction of 2-alkynylanisoles/sulfides with $SOCl_2$ and DMSO was conducted to conveniently furnish the biologically interesting 3-(methylthio)-benzo[*b*]furans/thiophenes *via* intramolecular cyclization. DMSO acts as a solvent as well as a sulfur source and can also be replaced with DMSO-d_6, enabling the incorporation of the SCD_3 moiety of DMSO-d_6 to the 3-position of the heterocyclic frameworks.

Background and Originality Content

As an important class of heteroaromatic molecules, benzofurans and benzothiophenes are frequently presented in many natural products,[1] synthetic functional molecules[2] and pharmaceutical agents.[3] They possess a broad range of biological properties including anticancer,[4] antimicrobial,[5] antiinflammatory,[6] antiviral[7] and antifungal activities.[8] Due to their potential utilities, many methods have been developed to achieve efficient construction of this two classes of privileged heterocyclic skeletons,[9] and great efforts have been devoted to the synthesis of benzofurans and benzothiophenes bearing substituents at 3-position. Notably, the construction of Csp^2-S bond has been widely reported, especially the synthesis of 3-chalcogen benzo[*b*]furans have received considerable attention during past decades.[10] As shown in Scheme 1, the majority of these methods use 2-(phenylethynyl)anisoles as substrates. For examples, Larock and coworkers[10a] reported the synthesis of 3-chalcogen benzo[*b*]furans from the reaction of 2-(phenylethynyl)anisole and 4-$NO_2C_6H_4SCl$ *via* electrophilic cyclization (Scheme 1a-i). Li,[10b] Zeni[10c] and Zhong[10d] realized the synthesis of 3-chalcogen benzo[*b*]furans by palladium-promoted cyclization of 2-alkynylphenols, $FeCl_3$-promoted annulation of 2-alkynylanisoles and the iodine-mediated annulation of 2-alkynylanisoles with disulfides, respectively (Scheme 1a-(ii-iv)). Wu and coworkers[10e] demonstrated the construction of 3-((trifluoromethyl)thio)benzofurans and 3-((trifluoromethyl)-thio)benzothiophenes *via* a $BiCl_3$-promoted reaction of trifluoromethanesulfanylamide and 1-methoxy-2-alkynylbenzenes or methyl(2-alkynylphenyl)sulfides (Scheme 1a-v). Lu[10f] developed a method for the synthesis of 3-aryl benzofuran thioethers by the I_2-catalyzed cross-coupling reaction of 3-substituted benzo[*b*]furans with aryl sulfonyl hydrazides *via* direct C–H functionalization (Scheme 1a-vi). Albeit these methods have their own merits in producing the corresponding substituted benzofurans and benzothiophenes, many of them require either expensive and air-sensitive metal catalysts or unstable sulfur sources such as sulfenyl halides and disulfides. Therefore, it is highly desirable to develop alternative efficient and eco-friendly methods for the synthesis of diversely functionalized 3-methylthio-benzo[*b*]furan derivatives from easily accessible, simple and "greener" starting materials.



Scheme 1 Methods for Synthesis of 3-Chalcogen Benzo[*b*]furans/Thiophenes

DMSO is not only a widely used aprotic polar solvent, but also a valuable reagent in many organic transformations.[11] For example, it has been used as an oxidant in several well-known name reactions, such as Swern oxidation[12] and Pfitzner-Moffatt

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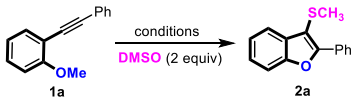
oxidation.[13] Furthermore, DMSO used as the source of $-CH_3$, –CHO, –SMe, $-SO_2Me$ and oxygen have also been seen in numerous synthetic methods.[14] However, less research[15] has been conducted on the introduction of sulfur moieties by using a combination of DMSO and activating reagents[16] including oxalyl chloride, trifluoroaceticanhydride, thionyl chloride and sulfur trioxide. Besides, to our knowledge, DMSO and DMSO-d_6 have seldom been used as sulfur source for introduction of –SMe or $-SCD_3$ moieties into benzo[*b*]furans/thiophenes. As DMSO is well recognized as an inexpensive, stable, low-toxicity and easy-to-handle reagent, it should be highly desirable if it can be used in methylthiolation of the biologically interesting benzo[*b*]furan/thiophene compounds.[17] Therefore, we became interested to investigate the reaction of 2-alkynylanisoles/sulfides with DMSO/DMSO-d_6 and $SOCl_2$, for synthesis of 3-(methylthio)-benzo[*b*]furans/thiophene compounds. Herein, we report our detailed studies.

Results and Discussion

Our study was initiated by treating 1-methoxy-2-(phenylethynyl)benzene **1a** (0.5 mmol) with DMSO (1 mmol) and oxalyl chloride as the additive for 0.5 h at 25 °C under air. From this reaction, 3-(methylthio)-2-phenylbenzofuran **2a** was obtained in 69% and 1-(2-methoxyphenyl)-2-phenylethane-1,2-dione was afforded in 5% yield, respectively (Table 1, entry 1). Encouraged by the remarkable biological activities associated with benzofurans, we were interested in establishing optimal conditions for synthesis of product **2a**.

Table 1 Optimization on the Reaction Conditions[a]



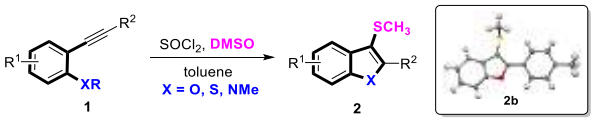
1a 2a

entry	activator	solvent	time (h)	yield (%)[b]
1	$(COCl)_2$	DMSO	1	69
2	TFAA	DMSO	12	trace
3	Ac_2O	DMSO	12	0
4	TsCl	DMSO	6	65
5	AcCl	DMSO	12	20
6	$SOCl_2$	DMSO	0.5	72
7	$SOCl_2$	DCE	12	12
8	$SOCl_2$	MeOH	12	35
9	$SOCl_2$	EtOAc	12	trace
10	$SOCl_2$	CH_3CN	3	73
11	$SOCl_2$	1,4-dioxane	12	22
12	$SOCl_2$	toluene	3	76
13	$SOCl_2$	THF	12	20
14	$SOCl_2$	DMF	1	14
15	$SOCl_2$	toluene	1	81
16[c]	$SOCl_2$	toluene	1	85
17[d]	$SOCl_2$	toluene	1	80
18[e]	$SOCl_2$	toluene	1	78

[a] Reaction conditions: **1a** (0.5 mmol), activator (2 equiv) and DMSO (2 equiv) in solvent (2 mL), stirred at 25 °C, unless otherwise stated. [b]Isolated yield. [c]Solvent (0.5 mL) was applied. [d]Activator (4 equiv) was added. [e]Stirred at 50 °C.

First, different activators such as TFAA, Ac_2O, TsCl, AcCl and $SOCl_2$ were screened (entries 2–6). It turned out that the reaction using $SOCl_2$ could improve the yield of product **2a** to72% (entry 6). Next, screening of different solvents including DCE, MeOH, EtOAc, CH_3CN, 1,4-dioxane, toluene, THF and DMF revealed that toluene is the most efficient solvent for the formation of product **2a** (entries 7–14 *vs* entry 6). In addition, by reducing the amount of toluene from 2 mL to 1 mL, a higher yield of product **2a** can be obtained due to the increased reaction concentration (0.25 mol/L to 0.5 mol/L) (entry 15). Further reducing the amount of toluene to 0.5 mL (1 mol/L) can secure the formation of product **2a** in 85% yield as the only product (entry 16). Further studies showed that when increasing the amount of $SOCl_2$ to 4 equiv, the yield of product **2a** was reduced to 80% (entry 17). Temperature study indicated that when the reaction was operated at 50 °C, the yield of product **2a** was decreased to 78% (entry 18). Thus, the following conditions for the selective formation of product **2a** were established: DMSO (2 equiv) and $SOCl_2$ (2 equiv) in toluene (0.5 mL) at 25 °C under air for 1 h.

Table 2 Substrate Scope Studies for Synthesis of **2**[a]



1 2

entry	substrate	product	yield (%)[b]
1	**1a**, R = Me, R^2 = Ph	**2a**, R^2 = Ph	85
2	**1a'**, R = H, R^2 = Ph	**2a**, R^2 = Ph	81
3	**1b**, R = Me, R^2 = Ph(4-Me)	**2b**, R^2 = Ph(4-Me)	86
4	**1c**, R = Me, R^2 = Ph(4-OMe)	**2c**, R^2 = Ph(4-OMe)	89
5	**1d**, R = Me, R^2 = Ph(4-F)	**2d**, R^2 = Ph(4-F)	82
6	**1e**, R = Me, R^2 = Ph(4-Cl)	**2e**, R^2 = Ph(4-Cl)	82
7	**1f**, R = Me, R^2 = Ph(4-Ph)	**2f**, R^2 = Ph(4-Ph)	76
8	**1g**, R = Me, R^2 = Ph(3-Me)	**2g**, R^2 = Ph(3-Me)	74
9	**1h**, R = Me, R^2 = Ph(2-Me)	**2h**, R^2 = Ph(2-Me)	81
10	**1i**, R = Me, R^2 = Ph(2-Cl)	**2i**, R^2 = Ph(2-Cl)	80
11	**1j**, R = Me, R^2 = 2-thienyl	**2j**, R^2 = 2-thienyl	65
12	**1k**, R = Me, R^2 = cyclopropyl	**2k**, R^2 = cyclopropyl	83
13	**1l**, R^1 = (4-Me)	**2l**, R^1 = (4-Me)	81
14	**1m**, R^1 = (4-Cl)	**2m**, R^1 = (4-Cl)	78
15	**1n**, R^2 = Ph	**2n**, R^2 = Ph	78
16	**1o**, R^2 = Ph(4-Cl)	**2o**, R^2 = Ph(4-Cl)	79
17	**1p**, R^2 = Ph(3-Me)	**2p**, R^2 = Ph(3-Me)	76
18	**1q**, R^2 = Ph(3-Cl)	**2q**, R^2 = Ph(3-Cl)	71
19	**1r**, R^2 = Ph(2-Me)	**2r**, R^2 = Ph(2-Me)	73
20	**1s**, R^2 = TMS	**2s**, R^2 = Cl	86
21	**1s'**, R^2 = H	**2s**, R^2 = Cl	81
22	**1t**, R = H	**2t**, R = H	0
23	**1t'**, R = Me	**2t**, R = Me	0

[a]Reaction conditions: **1** (0.5 mmol), $SOCl_2$ (1 mmol), DMSO (1 mmol) and toluene (0.5 mL) stirred at 25 °C for 1 h. [b]Isolated yield.

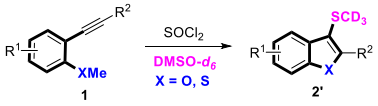
With the optimized reaction conditions established, the substrate scope for the synthesis of **2** was studied. First, the suitability of diversely substituted 2-alkynylanisoles **1** was studied by using DMSO as sulfur source. The results listed in Table 2 showed that when 2-(phenylethynyl) anisole or

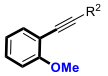
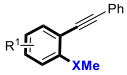
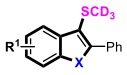
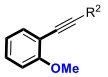
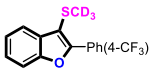
2-(phenylethynyl)phenol reacted as substrates with DMSO, respectively, the same product **2a** was obtained in good yields (entries 1-2). Next, when R is a methyl group, substrate **1** bearing either an electron-donating group (Me or MeO), an electron-withdrawing group (F, Cl, Br), or a phenyl group on the right phenyl ring could smoothly afford the corresponding products **2b-i** in yields ranging from 74 to 89% (entries 3-10). Moreover, the structure of **2b** was undoubtedly confirmed by X-ray diffraction analysis.[18] Meanwhile, it is worthy to note that the electronic nature of the phenyl moiety has shown effect on the outcome of this reaction since substrates bearing EDGs generally gave higher yields than those bearing EWGs (**2b-c** and **2g-h** *vs* **2d-f** and **2i**). 2-(2-Thienylethynyl)-anisole (**1j**) and 1-(cyclopropylethynyl)-(cyclopropylethynyl)-anisole (**1k**) were also suitable for this reaction, affording products **2j** and **2k** in a yield of 65% and 83%, respectively (entries 11-12). When substrate **1** bearing methyl group or chloro group on the left phenyl ring was applied, the reaction of substrates **1l** or **1m** with DMSO proceeded smoothly to afford product **2l** or **2m** in good yield respectively (entries 13-14),. Next, we tried to expand substrate scope of substrates **1** from 2-alkynylanisoles to 2-alkynylsulfides. We were pleased to find that all the methyl(2-(phenylethynyl)phenyl)sulfide substrates could react smoothly under standard reaction conditions to give target products **2n-r** in satisfactory yields (entries 15-19). Interestingly, trimethyl((2-(methylthio)phenyl)ethynyl)silane **1s** and (2-ethynylphenyl)(methyl)sulfide **1s'** could not lead to the expected substituted products. Instead, they both produced the chlorinated product **2s** in good yield (entries 20-21).[19] To our disappointment, when *N*-methyl-2-(phenylethynyl)anilines (**1t**) or *N,N*-dimethyl-2-(phenylethynyl)aniline (**1t'**) was subjected to the standard conditions, no desired corresponding 3-methylthio-indole product could be obtained in each case (entries 22-23). This result might indicate that the method was not applicable to the synthesis of indole analogue.

In recent years, the development of deuterated drugs has received extensive attention from both academia and industries.[20] In this regard, we were interested to investigate whether DMSO could be replaced with its deuterated counterpart, namely, DMSO-d_6 to realize the deuterium modification of 3-(methylthio)benzofurans/benzothiophenes **2'**. The suitability of a range of 2-alkynylanisoles/sulfides **1** for the formation of **2'** was studied by using DMSO-d_6 as sulfur source as well as solvent.[21] The results listed in Table 3 indicated that all substrates **1** employed in this reaction smoothly afforded the corresponding product **2'** in moderate to good yields. It was observed that various functional groups on the right phenyl ring, such as methyl, methoxy, chloro, trifluoromethyl, or phenyl groups, were well tolerated, resulting in the efficient formation of products **2a'-h'** and **2u** (entries 1-7 and 12). 1-(Cyclopropylethynyl)-2-methoxybenzene **1k** also reacted smoothly with DMSO-d_6 to give target compounds **2k'** in 84% yield (entry 8). Furthermore, substrate **1** bearing either an EDG such as methyl group, or an EWG such as chloro group, on the left phenyl ring could afford the corresponding products **2l'** and **2m'** in good yield (entries 9-10). To our pleasant, the protocol was also applicable to the synthesis of the corresponding deuterated benzothiophene product, as the reaction of 2-alkynylsulfide with DMSO-d_6 afforded **2n'** in a yield of 74% (entry 11).

Based on the aforementioned experimental results and previous reports,[22] we proposed possible mechanism for the formation of 3-methylthio-benzo[*b*]furan **2a** (Scheme 2). First, the reaction of DMSO with $SOCl_2$ gave the reactive CH_3SCl **B** *in situ,* via the key dimethylsulfochlorine cation **A,** through an interrupted Pummerer process.[23] Then, the electrophilic addition of the electrophilic CH_3SCl **B** to **1a** afforded the cyclic sulfonium cation **D** via allene intermediate **C**.[24, 25] Intermediate **D** favoured 5-*exo-trig* annulation to give oxonium intermediate **E**, which is converted to the target product **2a** via the removal of the methyl group in the presence of Cl^-.

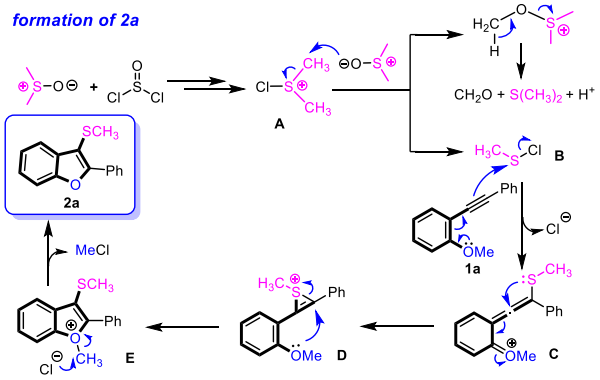
Table 3 Substrate Scope for Synthesis of **2'**[a]



entry	substrate	product	yield (%)[b]
			
1	**1a**, R^2 = Ph	**2a'**, R^2 = Ph	81
2	**1b**, R^2 = Ph(4-Me)	**2b'**, R^2 = Ph(4-Me)	82
3	**1c**, R^2 = Ph(4-OMe)	**2c'**, R^2 = Ph(4-OMe)	85
4	**1e**, R^2 = Ph(4-Cl)	**2e'**, R^2 = Ph(4- Cl)	80
5	**1f**, R^2 = Ph(4-Ph)	**2f'**, R^2 = Ph(4- Ph)	64
6	**1g**, R^2 = Ph(3-Me)	**2g'**, R^2 = Ph(3-Me)	74
7	**1h**, R^2 = Ph(2-Me)	**2h'**, R^2 = Ph(2-Me)	71
8	**1k**, R^2 = cyclopropyl	**2j'**, R^2 = cyclopropyl	84
			
9	**1l**, X = O, R^1 = (4-Me)	**2l'**, R^1 = (4-Me)	78
10	**1m**, X = O, R^1 = (4-Cl)	**2m'**, R^1 = (4-Cl)	76
11	**1n**, X = S, R^1 = H	**2n'**, R^1 = H	74
			
12	**1u**, R^2 = Ph(4-CF_3)	**2u'**, R^2 = Ph(4-CF_3)	69

[a]Reaction conditions: **1** (0.5 mmol), $SOCl_2$ (1 mmol), DMSO-d_6 (0.5 mL) stirred at 25 °C for 1h. [b]Isolated yield.

Scheme 2 Proposed Mechanism for the Formation of **2a**



Finally, to explore whether this method is suitable for gram-scale synthetic purpose, 10 mmol of **1a** was reacted with DMSO under standard reaction conditions. We were pleased to find that the reaction proceeded smoothly to afford **2a** in a yield of 78% (not shown).

Conclusions

In summary, we have developed a novel method for the synthesis of the biologically interesting 3-methylthio-benzo[*b*]furans/benzo[*b*]thiophenes *via* intramolecular cyclization of 2-alkynylanisoles/sulfides mediated by DMSO and $SOCl_2$. Strikingly, the readily available, cheap and "greener" DMSO can be used as sulfur source and oxidant to

introduce the biologically interesting methylthio group into the two important heterocyclic skeletons. Furthermore, DMSO can also be replaced with DMSO-d_6, allowing the incorporation of SCD_3 moiety into the 3-position of benzofuran skeleton. The presence of both heterocyclic skeleton and SMe/SCD_3 moiety might render the products valuable biological activities. Further studies on the reaction application are in progress in our lab.

Experimental

General Information. ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz or 600 MHz spectrometer at 25 °C. Chemical shifts values are given in ppm and referred as the internal standard to TMS: 0.00 ppm. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane, and were reported as s (singlet), d (doublet), t (triplet), q (quadruple), dd (doublet of doublet), m (multiplet), etc. The coupling constants J, are reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. Melting points were determined with a Micromelting point apparatus. TLC plates were visualized by exposure to ultraviolet light. Reagents and solvents were purchased as reagent grade and were used without further purification. All reactions were performed in standard glassware, heated at 70 °C for 3 h before use. The starting materials **1** were prepared according to literature methods.[10b] *N*-Methyl-2-(phenylethynyl)aniline (**1t**) and *N,N*-dimethyl-2-(phenylethynyl)aniline (**1t'**) were prepared by 2-iodo-anilines and ethynylbenzene.[26] Flash column chromatography was performed over silica gel (200-300 m) using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE).

General Procedure for the Synthesis of 2. To a solution of substrate **1** (0.5 mmol) and DMSO (1 mmol) in toluene (0.5 mL) was slowly added $SOCl_2$ (1.0 mmol). The mixture was kept stirring at 25 °C until TLC indicated the total consumption of substrate **1**. Then the reaction mixture was quenched with saturated aq. $NaHCO_3$ (10 mL), extracted with EtOAc (20 mL × 3). The combined organic phase was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel chromatography using EtOAc/PE as eluent to afford products **2**.

3-(Methylthio)-2-phenylbenzofuran (2a)[22b]

Following the general procedure, **2a** was purified by silica gel chromatography (5% EtOAc/PE). Colorless liquid (102 mg, 85%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29-8.28 (m, 2H), 7.70 (dd, J = 6.6, 1.8 Hz, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.37 (t, J = 7.8 Hz, 1H), 7.32-7.27 (m, 2H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.3, 153.7, 131.2, 130.4, 129.1, 128.6, 127.3, 125.1, 123.4, 120.1, 111.4, 109.3, 18.5; HRMS (ESI) calcd for $C_{15}H_{13}OS^+$ [M+H$^+$] 241.0682, found 241.0689. 2-(Phenylethynyl)phenol was used as substrate, yield: 98 mg, 81%.

3-(Methylthio)-2-(*p*-tolyl)benzofuran (2b)

Following the general procedure, **2b** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (109 mg, 86%); m.p. 51-52 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.32 (dd, J = 7.8, 1.2 Hz, 1H), 8.22 (d, J = 7.8 Hz, 1H), 8.07 (dd, J = 3.6, 1.2 Hz, 1H), 7.85 - 7.82 (m, 1H), 7.55-7.51 (m, 2H), 7.16 (dd, J = 5.4, 4.8 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.8, 152.5, 138.6, 135.3, 134.0, 131.4, 131.3, 129.9, 128.1, 126.9, 125.5, 120.4, 108.0, 18.6; HRMS (ESI) calcd for $C_{16}H_{15}OS^+$ [M+H$^+$] 255.0838, found 255.0839.

2-(4-Methoxyphenyl)-3-(methylthio)benzofuran (2c)

Following the general procedure, **2c** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (120 mg, 89%); m.p. 56-57 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, J = 9.0 Hz, 2H), 7.66 (dd, J_1 = 7.2 Hz, J_2 = 4.2 Hz, 1H), 7.46-7.44 (m, 1H), 7.24-7.26 (m, 2H), 6.95 (d, J = 9.0 Hz, 2H), 3.77 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.3, 155.6, 153.6, 131.4, 128.9, 124.7, 123.2, 123.1, 119.8, 114.1, 111.3, 107.4, 55.4, 18.5; HRMS calcd for $C_{16}H_{15}O_2S^+$ 271.0787 [M+H]$^+$, found 271.0790.

2-(4-Fluorophenyl)-3-(methylthio)benzofuran (2d)

Following the general procedure, **2d** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (105 mg, 82%); m.p. 59-60 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29-8.24 (m, 2H), 7.70-7.68 (m, 1H), 7.49-7.46 (m, 1H), 7.31-7.28 (m, 2H), 7.16-7.12 (m, 2H), 2.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (d, $^1J_{C\text{-}F}$ = 248.6 Hz), 154.3, 153.6, 131.1, 129.3 (d, $^3J_{C\text{-}F}$ = 8.1 Hz), 126.6 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 125.1, 123.3, 120.1, 115.7 (q, $^2J_{C\text{-}F}$ = 21.5 Hz), 111.4, 108.9, 18.4; HRMS calcd for $C_{15}H_{12}FOS^+$ 259.0587 [M+H], found 259.0588.

2-(4-Chlorophenyl)-3-(methylthio)benzofuran (2e)

Following the general procedure, **2e** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (112 mg, 82%); m.p. 63-64°C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 7.8 Hz, 1H), 7.42-7.41 (m, 2H), 7.32-7.29 (m, 2H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ.154.1, 153.7, 134.8, 131.0, 128.8, 128.4, 125.3, 123.4, 120.1, 111.4, 109.8, 18.4; HRMS calcd for $C_{15}H_{12}{}^{35}ClOS^+$ 275.0292 [M+H]$^+$, found 275.0296.

2-([1,1'-Biphenyl]-4-yl)-3-(methylthio)benzofuran (2f)

Following the general procedure, **2f** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (120 mg, 76%); m.p. 81-83 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 7.70 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 1H), 7.67 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 7.61 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H), 7.48 (dd, J_1 = 6.6 Hz, J_2 = 1.2 Hz, 1H), 7.41 (t, J = 7.8 Hz, 2H), 7.33-7.25 (m, 3H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.1, 153.8, 141.6, 140.5, 131.4, 129.3, 129.0, 127.8, 127.7, 127.23, 127.15, 125.2, 123.3, 120.1, 111.4, 18.5; HRMS calcd for $C_{21}H_{17}OS^+$ 317.0995 [M+H]$^+$, found: 317.0999.

3-(Methylthio)-2-(*m*-tolyl)benzofuran (2g)

Following the general procedure, **2g** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (94 mg, 74%); m.p. 53-55 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.11 (dd, J = 7.9, 0.5 Hz, 1H), 8.06 (s, 1H), 7.70-7.68 (m, 1H), 7.50-7.46 (m, 1H), 7.34 (t, J = 7.7 Hz, 1H), 7.30-7.25 (m, 2H), 7.18 (dd, J = 7.5, 0.5 Hz, 1H), 2.42 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.6, 153.8, 138.2, 131.3, 130.3, 129.9, 128.5, 127.9, 125.0, 124.6, 123.2, 120.1, 111.4, 109.2, 21.7, 18.5; HRMS calcd for $C_{16}H_{15}OS^+$ 255.0838 [M+H]$^+$, found: 255.0843.

3-(Methylthio)-2-(*o*-tolyl)benzofuran (2h)

Following the general procedure, **2h** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (102 mg, 81%); m.p. 51-52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.71 (m, 1H), 7.55-7.49 (m, 2H), 7.39-7.27 (m, 5H), 2.40 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.5, 154.3, 138.2, 131.1, 130.7, 130.0, 129.7, 129.5, 125.5, 124.8, 123.1, 120.0, 111.6, 110.8, 20.6, 18.4; HRMS calcd for $C_{16}H_{15}OS^+$ 255.0838 [M+H]$^+$, found: 255.0846.

2-(2-Chlorophenyl)-3-(methylthio)benzofuran (2i)

Following the general procedure, **2i** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (109 mg, 80%); m.p. 58-59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 6.4, 2.3 Hz, 1H), 7.58-7.49 (m, 3H), 7.39-7.30 (m, 4H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 154.5, 134.5, 132.7, 131.1, 130.2, 129.7, 129.4, 126.6, 125.3, 123.3, 120.3, 112.5, 111.8, 18.2; HRMS calcd for $C_{15}H_{12}{}^{35}ClOS^+$ 275.0292 [M+H]$^+$, found 275.0299.

3-(Methylthio)-2-(thiophen-2-yl)benzofuran (2j)

Following the general procedure, **2j** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (80 mg, 65%); m.p. 46-47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 3.7, 1.1 Hz, 1H), 7.67-7.65 (m, 1H), 7.48-7.46 (m, 1H), 7.42 (dd, J = 5.0, 1.1 Hz, 1H), 7.32-7.26 (m, 2H), 7.13 (dd, J = 5.0, 3.8 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 152.5, 131.8, 130.9, 127.6, 127.4, 127.0, 125.0, 123.4, 119.7, 111.3, 107.8, 18.3; HRMS calcd for $C_{11}H_{13}OS_2^+$ 247.0246 [M+H]$^+$, found 247.0253.

2-Cyclopropyl-3-(methylthio)benzofuran (2k)

Following the general procedure, **2k** was purified by silica gel chromatography (PE). Colorless liquid (85 mg, 83%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 1H), 7.24-7.18 (m, 2H), 2.45-2.41 (m, 1H), 2.33 (s, 3H), 1.17-1.14 (m, 2H), 1.06-1.03 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.6, 153.3, 130.5, 123.6, 122.9, 118.7, 110.9, 107.5, 18.9, 8.4, 7.9; HRMS calcd for $C_{12}H_{13}OS^+$ 205.0682 $[M+H]^+$, found 205.0693.

5-Methyl-3-(methylthio)-2-phenylbenzofuran (2l)[27]

Following the general procedure, **2l** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (103 mg, 81%); m.p. 60-63 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.26 (m, 2H), 7.44-7.49 (m, 3H), 7.37 (d, *J* = 8.6 Hz, 2H), 7.11 (dd, *J* = 8.3, 1.4 Hz, 1H), 2.47 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 152.2, 132.8, 131.3, 130.5, 128.9, 128.56, 127.3, 126.4, 119.8, 110.9, 108.9, 21.5, 18.5; HRMS calcd for $C_{16}H_{15}OS^+$ 255.0838 $[M+H]^+$, found: 255.0849.

5-Chloro-3-(methylthio)-2-phenylbenzofuran (2m)

Following the general procedure, **2m** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (100 mg, 73%); m.p. 67-68 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.65 (d, *J* = 2.1 Hz, 1H), 7.47-7.44 (m, 2H), 7.40-7.36 (m, 2H), 7.24 (dd, *J* = 8.6, 2.2 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.8, 152.0, 132.7, 129.9, 129.4, 129.0, 128.6, 127.3, 125.2, 119.7, 112.4, 108.9, 18.4; HRMS calcd for $C_{15}H_{12}{}^{35}ClOS^+$ 275.0292 $[M+H]^+$, found 275.0301.

3-(Methylthio)-2-phenylbenzo[*b*]thiophene (2n)

Following the general procedure, **2n** was purified by silica gel chromatography (5% EtOAc/PE). A white liquid (100 mg, 78%) ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.0 Hz, 2H), 7.43 (dd, *J* = 11.6, 4.1 Hz, 3H), 7.38-7.36 (m, 1H), 7.34 (td, *J* = 7.8, 1.2 Hz, 1H), 2.20 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 146.2, 141.3, 138.5, 134.0, 130.0, 128.7, 128.5, 125.1, 124.9, 123.6, 122.4, 19.1; HRMS calcd for $C_{15}H_{13}S_2^+$ 257.0453 $[M+H]^+$, found 257.0458.

2-(4-Chlorophenyl)-3-(methylthio)benzo[*b*]thiophene (2o)

Following the general procedure, **2o** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (114 mg, 79%); m.p. 55-57 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.0, 0.4 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.70-7.67 (m, 2H), 7.47-7.35 (m, 4H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 141.2, 138.3, 134.7, 132.4, 131.2, 128.7, 125.2, 125.0, 124.1, 123.7, 122.4, 19.0; HRMS calcd for $C_{15}H_{12}ClS_2^+$ 291.0063 $[M+H]^+$, found 291.0070.

3-(Methylthio)-2-(*m*-tolyl)benzo[*b*]thiophene (2p)

Following the general procedure, **2p** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (102 mg, 76%); m.p. 59-61 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.58-7.54 (m, 2H), 7.43 (td, *J* = 7.6, 0.8 Hz, 1H), 7.35-7.31 (m, 2H), 7.19 (d, *J* = 7.6 Hz, 1H), 2.40 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4, 141.4, 138.5, 138.2, 133.9, 130.6, 129.5, 128.4, 127.1, 125.0, 125.9, 123.6, 123.5, 122.4, 21.6, 19.1; HRMS calcd for $C_{16}H_{15}S_2^+$ 271.0610 $[M+H]^+$, found 271.0613.

2-(3-Chlorophenyl)-3-(methylthio)benzo[*b*]thiophene (2q)

Following the general procedure, **2q** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (103 mg, 71%); m.p. 65-66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.0, 0.4 Hz, 1H), 7.76-7.78 (m, 2H), 7.61 (ddd, *J* = 5.4, 3.1, 1.7 Hz, 1H), 7.45-7.41 (m, 1H), 7.36-7.32 (m, 3H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 141.2, 138.4, 135.7, 134.4, 129.9, 129.7, 128.7, 128.2, 125.4, 125.1, 124.6, 123.8, 122.5, 19.1; HRMS calcd for $C_{15}H_{12}{}^{35}ClS_2^+$ 291.0063 $[M+H]^+$, found 291.0069.

3-(Methylthio)-2-(*o*-tolyl)benzo[*b*]thiophene (2r)

Following the general procedure, **2r** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (99 mg, 73%); m.p. 57-58 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.45 (td, *J* = 7.2, 0.6 Hz, 1H), 7.37-7.34 (m, 1H), 7.33 (dd, *J* = 11.6, 4.3 Hz, 2H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.24 (td, *J* = 7.8, 0.6 Hz, 1H), 2.26 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.7, 140.3, 139.2, 137.8, 133.5, 131.1, 130.2, 129.1, 125.5, 125.5, 124.9, 124.8, 123.3, 122.4, 20.4, 18.6; HRMS calcd for $C_{16}H_{15}S_2^+$ 271.0610 $[M+H]^+$, found 271.0623.

2-Chloro-3-(methylthio)benzo[*b*]thiophene (2s)

Following the general procedure, **2s** was purified by silica gel chromatography (5% EtOAc/PE). Colorless liquid (91 mg, 86%); ^{1}H NMR (600 MHz, $CDCl_3$) δ7.49 (d, *J* = 7.8, 1.2 Hz, 1H), 7.26 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.10 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.97 (td, *J* = 7.8, 1.2 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 139.7, 132.7, 127.9, 127.8, 125.7, 125.5, 121.8, 15.8; HRMS calcd for $C_9H_8{}^{35}ClS_2^+$ 214.9750 $[M+H]^+$, found 214.9756. 1-Ethynyl-2-methoxybenzene was used as substrate, yield: 87 mg, 81%.

General Procedure for the synthesis of 2'. To a solution of substrate **1** (0.5 mmol) in DMSO-d_6 (0.5 mL) was slowly added $SOCl_2$ (1.0 mmol). The mixture was kept stirring at 25 °C until TLC indicated the total consumption of substrate **1**. Then the reaction mixture was quenched with saturated aq. $NaHCO_3$ (10 mL), extracted with EtOAc (20 mL × 3). The combined organic phase was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel chromatography using EtOAc/PE as eluent to afford **2'**.

3-((Methyl-d_3)thio)-2-phenylbenzofuran (2a')

Following the general procedure, **2a'** was purified by silica gel chromatography (5% EtOAc/PE). Colorless liquid (98 mg, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.72-7.69 (m, 1H), 7.51-7.45 (m, 3H), 7.40-7.36 (m, 1H), 7.34-7.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 153.8, 131.3, 130.4, 129.1, 128.6, 127.4, 125. 1, 123.2, 120.1, 111.4, 109.2; HRMS (ESI) calcd for $C_{15}H_{10}D_3OS^+$ $[M + H^+]$ 244.0870, found 244.0878.

3-((Methyl-d_3)thio)-2-(*p*-tolyl)benzofuran (2b')

Following the general procedure, **2b'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (105 mg, 82%); m.p. 57-59 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 6.6 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.27-7.23 (m, 4H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.7, 153.7, 139.2, 131.4, 129.4, 127.7, 127.3, 124.9, 123.2, 120.0, 111.4, 108.4, 21.6; HRMS (ESI) calcd for $C_{16}H_{12}D_3OS^+$ $[M + H^+]$ 258.1026, found 258.1031.

2-(4-Methoxyphenyl)-3-((methyl-d_3)thio)benzofuran (2c')

Following the general procedure, **2c'** was purified by silica gel chromatography (5% EtOAc/PE); A white solid (116 mg, 85%); m.p. 66-68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.8 Hz, 2H), 7.57-7.55 (m, 1H), 7.47-7.45 (m, 1H), 7.31-7.27 (m, 2H), 6.99 (d, *J* = 9.0 Hz, 2H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 152.5, 149.2, 128.3, 127.9, 125.1, 123.3, 122.0, 118.6, 114.2, 111.2, 106.3, 55.4; HRMS (ESI) calcd for $C_{16}H_{12}D_3O_2S^+$ $[M + H^+]$ 274.0976, found 274.0977.

2-(4-Chlorophenyl)-3-((methyl-d_3)thio)benzofuran (2e')

Following the general procedure, **2e'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (110 mg, 80%); m.p. 67-69 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.36-7.30 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ ^{13}C NMR (151 MHz, $CDCl_3$) δ 154.1, 153.7, 134.9, 131.0, 128.8, 128.8, 128.4, 125.3, 123.3, 120.1, 111.4, 109.71; HRMS (ESI) calcd for $C_{15}H_9D_3{}^{35}ClOS^+$ $[M + H^+]$ 278.0480, found 278.0486.

2-([1,1'-Biphenyl]-4-yl)-3-((methyl-d_3)thio)benzofuran (2f')

Following the general procedure, **2f'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (102 mg, 64%); m.p. 73-74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.6 Hz, 2H), 7.70 (d, *J* = 8.6 Hz, 2H), 7.64-7.58 (m, 3H), 7.50-7.43 (m, 3H), 7.36-7.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 148.8, 141.5, 140.4, 129.0, 128.2, 128.2, 127.8, 127.3, 127.1, 126.7, 125.6, 123.5, 119.0, 111.5, 108.1, 100.0; HRMS (ESI) calcd for $C_{21}H_{14}D_3OS^+$ $[M + H^+]$ 320.1183, found 320.1187.

3-((Methyl-d_3)thio)-2-(*m*-tolyl)benzofuran (2g')

Following the general procedure, **2g'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (95 mg, 74%); m.p.

71-73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.37-7.26 (m, 3H), 7.19 (d, *J* = 7.6 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.7, 149.2, 138.4, 129.8, 129.2, 128.6, 128.2, 126.8, 125.5, 123.5, 123.4, 118.9, 111.4, 107.8, 21.7; HRMS (ESI) calcd for $C_{16}H_{12}D_3OS^+$ [M + H^+] 258.1026, found 258.1034.

3-((Methyl-*d*$_3$)thio)-2-(*o*-tolyl)benzofuran (2h')

Following the general procedure, **2h'** was purified by silica gel chromatography (5% EtOAc/PE). Colorless liquid (91 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.58 (m, 2H), 7.50-7.47 (m, 1H), 7.38-7.27 (m, 5H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 151.3, 138.2, 130.9, 130.5, 129.8, 128.1, 127.3, 125.7, 125.3, 123.4, 119.0, 111.6, 109.4, 20.5; HRMS (ESI) calcd for $C_{16}H_{12}D_3OS^+$ [M + H^+] 258.1026, found 258.1033.

2-Cyclopropyl-3-((methyl-*d*$_3$)thio)benzofuran (2k')

Following the general procedure, **2k'** was purified by silica gel chromatography (PE). Colorless liquid (87 mg, 84%); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.33 (dd, *J* = 7.2, 0.6 Hz, 1H), 7.25-7.19 (m, 2H), 2.43 (tt, *J* = 8.5, 5.1 Hz, 1H), 1.17-1.14 (m, 2H), 1.07-1.04 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.6, 153.3, 130.5, 123.5, 1229, 118.7, 110.8, 107.4, 8.34, 7.8; HRMS (ESI) calcd for $C_{12}H_{10}D_3OS^+$ [M + H^+] 208.0870, found 208.0877.

5-Methyl-3-((methyl-*d*$_3$)thio)-2-phenylbenzofuran (2l')

Following the general procedure, **2l'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (100 mg, 78%); m.p. 63-64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.26 (m, 2H), 7.49-7.44 (m, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.11 (dd, *J* = 8.3, 1.3 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 152.2, 132.8, 131.3, 130.5, 128.9, 128.6, 127.3, 126.4, 119.8, 110.9, 108.9, 21.5; HRMS (ESI) calcd for $C_{16}H_{12}D_3OS^+$ [M + H^+] 258.1026, found 258.1037.

5-Chloro-3-((methyl-*d*$_3$)thio)-2-phenylbenzofuran (2m')

Following the general procedure, **2m'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (105 mg, 76%); m.p. 64-65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 7.2, 1.6 Hz, 2H), 7.64 (d, *J* = 2.0 Hz, 1H), 7.47-7.43 (m, 2H), 7.40-7.35 (m, 2H), 7.23 (dd, *J* = 8.6, 2.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.7, 152.0, 132.8, 129.9, 129.4, 129.0, 128.6, 127.3, 125.3, 119.7, 112.4, 108.8; HRMS (ESI) calcd for $C_{15}H_9D_3{}^{35}ClOS^+$ [M + H^+] 278.0480, found 278.0487.

3-((Methyl-*d*$_3$)thio)-2-phenylbenzo[*b*]thiophene (2n')

Following the general procedure, **2n'** was purified by silica gel chromatography (5% EtOAc/PE). Colorless liquid (95 mg, 74%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.83-7.73 (m, 3H), 7.53-7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.34, 192.83, 158.81, 135.91, 134.04, 132.63, 130.05, 129.40, 128.81, 127.13, 125.05, 113.93, 77.33, 77.22, 77.02, 76.70, 56.12; HRMS calcd for $C_{15}H_{10}D_3S_2^+$ 260.0641 [M+H]$^+$, found 260.0647.

3-((Methyl-*d*$_3$)thio)-2-(4-(trifluoromethyl)phenyl)benzofuran (2u')

Following the general procedure, **2u'** was purified by silica gel chromatography (5% EtOAc/PE). A white solid (102 mg, 69%); m.p. 79-80 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.42 (d, *J* = 8.2 Hz, 2H), 7.94 (d, *J* = 8.3 Hz, 2H), 7.82-7.80 (m, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.47 (ddd, *J* = 8.3, 7.3, 1.3 Hz, 1H), 7.41 (td, *J* = 7.7, 0.9 Hz, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 153.3, 152.4, 133.2, 130.1, 129.0 (q, $^3J_{C\text{-}F}$ = 31.95 Hz), 127.4, 126.3, 125.7 (q, $^3J_{C\text{-}F}$ = 3.75 Hz), 124.0 (q, $^1J_{C\text{-}F}$ = 270.6 Hz), 123.9, 120.4, 111.7, 111.5; HRMS (ESI) calcd for $C_{16}H_9D_3F_3OS^+$ [M + H^+] 312.0744, found 312.0749.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

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Title **Synthesis of 3-Methylthio-benzo[*b*]furans/Thiophenes via Intramolecular Cyclization of 2-Alkynylanisoles/Sulfides Mediated by DMSO/DMSO-d_6 and SOCl2**

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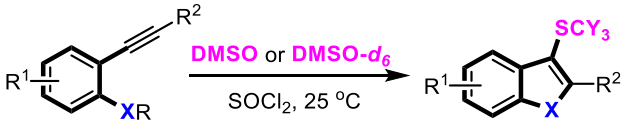
←Max. Table height 6 cm→

The "S" moiety was introduced from DMSO/DMSO-d_6



X = O, S; R = Me, H
R^1 = Me, Cl
R^2 = aryl, cyclopropyl, TMS, H

Y = H/D
31 examples
up to 89% yield

The reaction of 2-alkynylanisoles/sulfides with $SOCl_2$ and DMSO was conducted to conveniently furnish the biologically interesting 3-(methylthio)-benzo[*b*]furans/thiophenes *via* intramolecular cyclization. DMSO acts as a solvent as well as a sulfur source and can also be replaced with DMSO-d_6, enabling the incorporation of the SCD_3 moiety of DMSO-d_6 to the 3-position of the heterocyclic frameworks.