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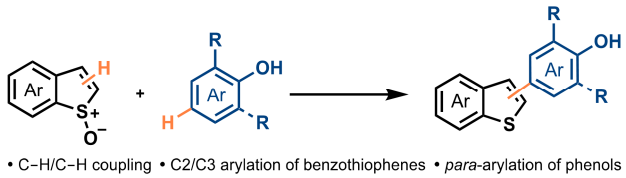

• C–H/C–H coupling • C2/C3 arylation of benzothiophenes • *para*-arylation of phenols

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Para-coupling of phenols with C2/C3-substituted benzothiophene *S*-oxides

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ABSTRACT

C2 and C3 Substituted benzothiophenes are common structures in medicinal and materials chemistry. The cross-coupling of phenols with benzothiophenes is a useful route towards these important molecules. In this report we reveal an efficient C–H/C–H-type cross-coupling of benzothiophenes, activated as their *S*-oxides, with phenols to give C2/C3 arylated benzothiophenes. Whereas previous reports describe cross-coupling at the *ortho*-position between phenols and sulfoxides, this procedure allows *para*-functionalization of phenols that typically have their *ortho* positions blocked.

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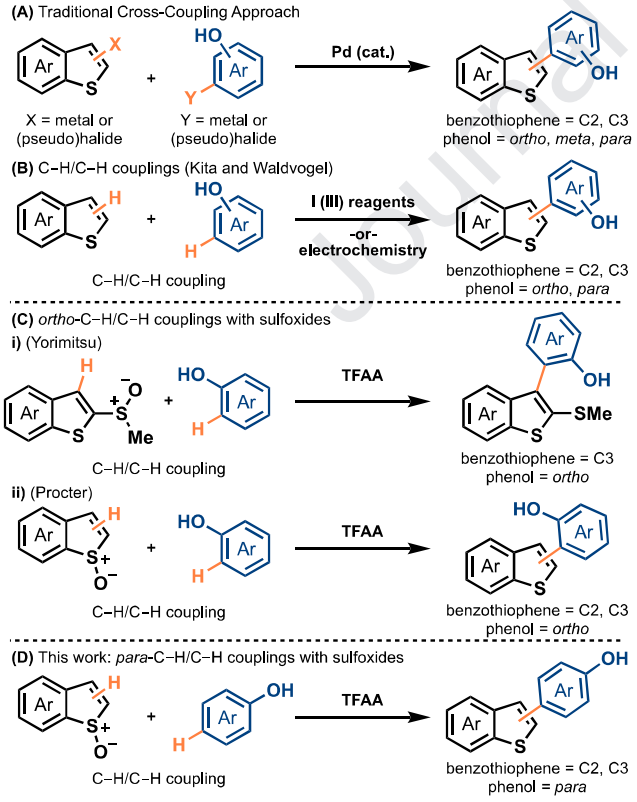
1. Introduction

Benzothiophene and phenol motifs combine to lend function to a range of important molecules. For example, raloxifene is an important drug molecule for the prevention and treatment of osteoporosis.[1] Other bioactive molecules that boast benzothiophene and phenol substructures include antibacterials and cancer treatments.[2] There also exists a range of useful organic materials, for example the benzothieno[3,2-*b*]benzofuran (BTBF) family, that is based on a benzothiophene-phenol containing core.[3]

The most common route to biaryls involves transition metal-catalyzed cross-coupling reactions. This strategy has been used to link phenols with benzothiophenes,[4] however, in many cases, additional steps are required for the protection/deprotection of the phenol hydroxyl group.[5] Furthermore, prefunctionalized starting materials (e.g. aryl halides/organometallics) are required in this route (Scheme 1A). The coupling of unfunctionalized phenols and benzothiophenes via C–H/C–H cross-coupling is a more direct route for heterobiaryl formation. Kita[6] and Waldvogel[7] have made key developments in this area by using iodonium reagents or electrochemistry to mediate cross-coupling (Scheme 1B). Another related example has been reported by You and co-workers who described C–H/C–H coupling between benzothiophenes and the phenol derivative, 2-phenoxypyridine.[8]

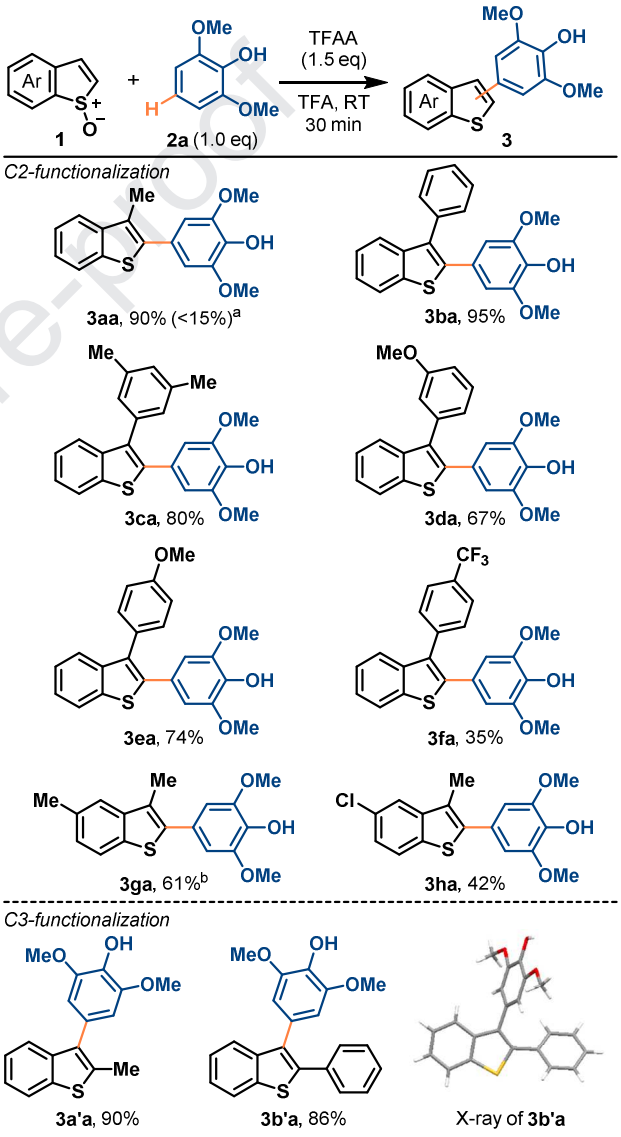
In recent years, interest has grown in the use of sulfoxides to mediate the functionalization of C–H bonds.[9] In particular, the Yorimitsu group (Scheme 1C, i)[10] and our group (Scheme 1C, ii)[11] have described sulfoxide-mediated coupling of benzothiophenes with phenols. A sequence of sulfoxide activation, interrupted



Scheme 1. Methods for the cross-coupling of benzothiophenes and phenols.

Pummerer reaction and [3.3]-sigmatropic rearrangement has been proposed to account for the selectivity of these reactions that provide *ortho*-functionalized phenols. More recently, we have applied this reactivity in the sulfoxide-catalyzed homocoupling and sulfoxide-mediated cross-couplings of phenols.[12]

In this report, we describe further studies on the use of sulfur oxidation to enable the C–H/C–H cross-coupling of benzothiophenes with phenols (Scheme 1D). We demonstrate that phenols undergo cross-coupling with benzothiophenes, activated as their *S*-oxides, in the presence of trifluoroacetic anhydride (TFAA). Substitution is tolerated at various positions on either coupling partner, including at both the C2 and C3 positions of the benzothiophene *S*-oxide. Importantly, this transformation can occur at the *para*-position of the phenol, whereas previous reports have involved only *ortho*-functionalization.[10,11] Despite this, we also demonstrate that coupling at the *ortho*-position of the phenol is tolerated in this system, including a method for difunctionalization in the preparation of alternating benzothiophene-phenol units.

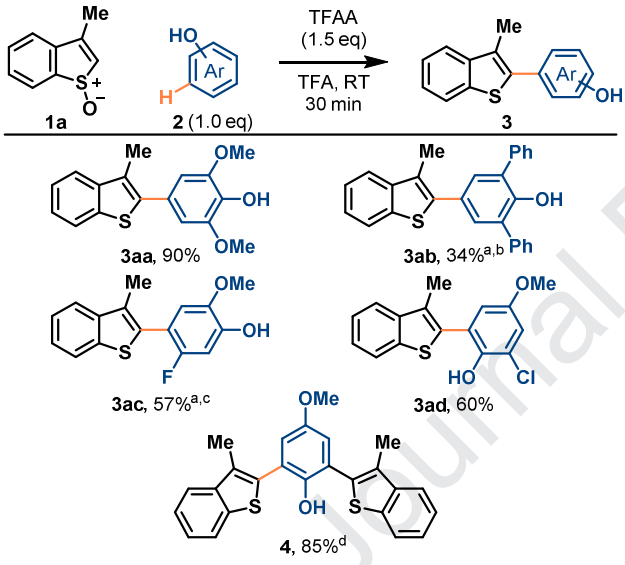


Scheme 2. Scope of the benzothiophene *S*-oxide in the C–H/C–H-type cross-coupling of benzothiophene *S*-oxides and phenols. Conditions: **1** (0.1 mmol, 1.0 eq), **2a** (0.1 mmol, 1.0 eq), TFAA (0.15 mmol, 1.5 eq), TFA (1.0 mL). [a] CH_2Cl_2 used as solvent. [b] NMR yield.

2. Results and discussion

We began our investigation by using phenol **2a** as a model substrate for the *para*-functionalization of phenols (Scheme 2).

Building on our previous reports,[11] we attempted the coupling of phenol **2a** with 3-methylbenzothiophene *S*-oxide **1a** in CH_2Cl_2, using TFAA as an activator. Under these conditions, <15% of the desired cross-coupled product **3aa** was obtained. Having previously reported that the *para*-functionalization of phenols can occur in trifluoroacetic acid (TFA),[12b] we also tested this process in TFA and were pleased to obtain 90% isolated yield of the desired product **3aa**. With suitable conditions in hand, we investigated the scope of the reaction with respect to the benzothiophene *S*-oxide **1**. The methyl group at C3 could be switched with a phenyl group without loss in reactivity; **3ba** was isolated in 95% yield. Various substituents on the phenyl group at C3 were also tolerated (**3ba**-**3fa**), however, the presence of electron-withdrawing substituents (e.g. CF_3) significantly lowered the yield of the reaction (**3fa**). Similarly, substitution at the C5 position of the benzothiophene was also tolerated (**3ga**, **3ha**), although electron-withdrawing substituents proved detrimental to reactivity. By using C2-substituted benzothiophene *S*-oxides, functionalization at the C3-position of the benzothiophene was also achieved. Both alkyl and phenyl substituted benzothiophene *S*-oxides were applicable (**3a'a**, **3b'a**). The *para*-selectivity of the reaction was confirmed by X-ray crystallographic analysis of **3b'a**.[13]



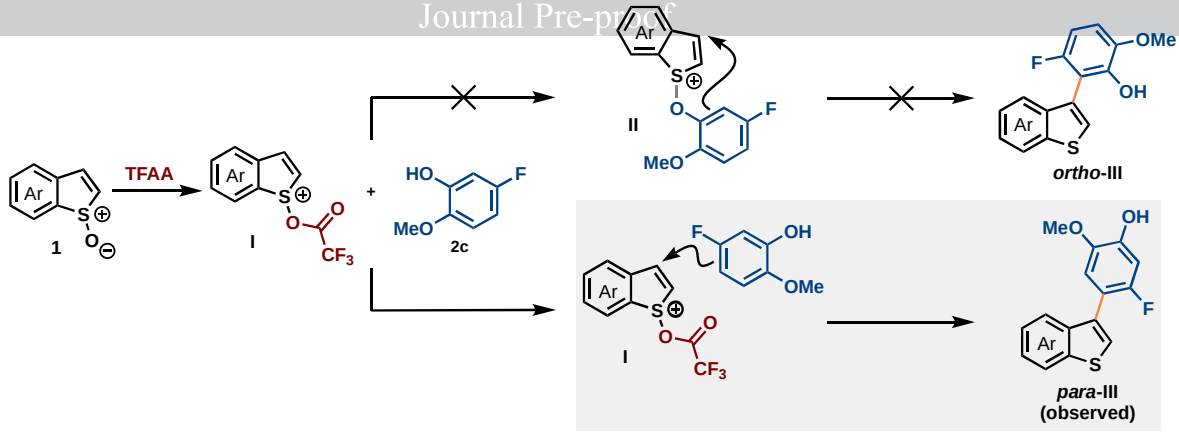
Scheme 3. Scope of the phenol partner in the C–H/C–H-type cross-coupling of benzothiophene *S*-oxides and phenols. Conditions: **1a** (0.1 mmol, 1.0 eq), **2** (0.1 mmol, 1.0 eq), TFAA (0.15 mmol, 1.5 eq), TFA (1.0 mL). [a] NMR yield. [b] 0.1 mL CH_2Cl_2 added. [c] **2c** (0.2 mmol, 2.0 eq). [d] **1a** (0.22 mmol, 2.2 equiv of benzothiophene *S*-oxide).

By investigating the scope of the phenolic coupling partner (Scheme 3), we found that other 2,6-disubstituted phenols were tolerated in the reaction, albeit the product was obtained in low yield (**3ab**). Impressively, 2,5-disubstituted phenol **2c**, which has the potential to undergo reaction at either the *ortho*- or *para*-position, provided the *para*-substituted product **3ac** with complete regioselectivity. This example provides an insight into the mechanism of the reaction (*vide infra*). *Ortho*-coupling at phenol was also possible using this reaction system, as shown in the preparation of **3ad**.[14] Interestingly, when using 4-substituted phenols, twofold *ortho*-functionalization was observed to give product **4**. This suggests that the current method is more reactive than previous procedures, which are selective for mono-functionalization.[10,11,15] Furthermore, the alternating arene-(benzo)thiophene unit, as seen in product **4**, is a common motif in organic materials.[16]

Our mechanistic hypothesis for this reaction is displayed in Scheme 4, using phenol **2c** as a model substrate. Firstly, as the addition of (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) did not significantly impact the efficiency of the reaction, we believe a pathway involving radical intermediates is unlikely.[17] We propose that this reaction is initiated by reaction of the benzothiophene *S*-oxides **1** with TFAA to give the activated sulfoxides **I**. In previous reports, we and others have suggested that activated sulfoxides can undergo an interrupted Pummerer reaction to give aryloxysulfonium salt intermediates **II**.[10,11] This species is then susceptible to *ortho*-functionalization of the phenol via [3,3]-sigmatropic rearrangement and aromatization to give products ***ortho*-III**. However, in the current report, the reaction of **2c** does not provide products of *ortho*-functionalization. This suggests another mechanism is operating. We propose that the activated sulfoxides **I** can engage directly at the *para*-position of phenol **2c** to give products ***para*-III** by a vinylogous Pummerer-type mechanism. In order to obtain C2-substituted benzothiophene products when a C3 substituent is present, direct C3 addition may be followed by subsequent 1,2-migration to C2.[11b,18] Alternatively, a direct, extended vinylogous Pummerer addition to C2 is also possible.

3. Conclusion

We have described a novel method for the union of benzothiophenes and phenols that relies on the activation of the benzothiophene partner by sulfur oxidation, and constitutes a formal C–H/C–H cross-coupling process. The reaction is selective for functionalization at the *para* position of the phenol partner and can give either C2 or C3 arylated benzothiophenes. In comparison to related sulfoxide-mediated cross-couplings, the observed *para*-selectivity suggests the reaction proceeds through a mechanistically distinct vinylogous Pummerer pathway.



Scheme 4. Proposed mechanism for the para-selective cross-coupling of benzothiophene *S*-oxides and phenols.

4. Experimental section

4.1. General Procedure

Benzothiophene (**1**, 0.1 mmol, 1 equiv) and phenol (**2**, 0.1 mmol, 1.0 equiv) were dissolved in TFA (1 mL, 0.1 M) in an oven-dried tube flushed with N_2. TFAA (20 *u*L, 0.15 mmol, 1.5 equiv) was then added at room temperature and the reaction stirred for 30 min. Saturated aqueous $NaHCO_3$ was then added and the aqueous phase was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with *n*-hexane/EtOAc.

*2,6-Dimethoxy-4-(3-methylbenzo[b]thiophen-2-yl)phenol (**3aa**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.47 (s, 3H, C*H*$_3$), 3.94 (s, 6H, OC*H*$_3$), 5.62 (s, 1H, O*H*), 6.76 (s, 2H, ArC*H*), 7.34 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H, ArC*H*), 7.41 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H, ArC*H*), 7.71 (d, *J* = 7.6 Hz, 1H, ArC*H*), 7.82 (d, *J* = 7.7 Hz, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.9 (*C*H$_3$), 56.5 (O*C*H$_3$), 106.8 (Ar*C*H), 122.1 (Ar*C*H), 122.2 (Ar*C*H), 124.3 (Ar*C*H), 124.4 (Ar*C*H), 125.9 (Ar*C*), 127.1 (Ar*C*), 134.8 (Ar*C*), 138.4 (Ar*C*), 138.7 (Ar*C*), 141.3 (Ar*C*), 147.1 (Ar*C*) ppm.

*2,6-Dimethoxy-4-(3-phenylbenzo[b]thiophen-2-yl)phenol (**3ba**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.66 (s, 6H, OC*H*$_3$), 5.54 (s, 1H, O*H*), 6.56 (s, 2H, ArC*H*), 7.31-7.45 (m, 7H, ArC*H*), 7.55-7.58 (m, 1H, ArC*H*), 7.85-7.87 (m, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 56.1 (O*C*H$_3$), 106.6 (Ar*C*H), 122.1 (Ar*C*H), 123.2 (Ar*C*H), 124.56 (Ar*C*H), 124.60 (Ar*C*H), 125.4 (Ar*C*), 127.5 (Ar*C*H), 128.9 (Ar*C*H), 130.6 (Ar*C*H), 132.7 (Ar*C*), 134.7 (Ar*C*), 136.2 (Ar*C*), 138.4 (Ar*C*), 139.8 (Ar*C*), 141.2 (Ar*C*), 146.9 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{22}H_{17}O_3S$ (M-H$^+$), 361.0904; found 361.0901.

*4-(3-(3,5-Dimethylphenyl)benzo[b]thiophen-2-yl)-2,6-dimethoxyphenol (**3ca**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.32 (s, 6H, C*H*$_3$), 3.68 (s, 6H, OC*H*$_3$), 5.52 (s, 1H, O*H*), 6.61 (s, 2H, ArC*H*), 6.98-7.01 (m, 3H, ArC*H*), 7.30-7.33 (m, 2H, ArC*H*), 7.51-7.54 (m, 1H, ArC*H*), 7.83-7.85 (m, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = (1 × ArCH missing) 21.4 (*C*H$_3$), 56.1 (O*C*H$_3$), 106.5 (Ar*C*H), 122.0 (Ar*C*H), 123.4 (Ar*C*H), 124.5 (Ar*C*H), 125.6 (Ar*C*), 128.2 (Ar*C*H), 129.1 (Ar*C*H), 133.0 (Ar*C*), 134.6 (Ar*C*), 136.1 (Ar*C*), 138.3 (Ar*C*), 138.4 (Ar*C*), 139.2 (Ar*C*), 141.6 (Ar*C*), 146.8 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{24}H_{23}O_3S$ (M+H$^+$), 391.1349; found 391.1352.

*2,6-Dimethoxy-4-(3-(3-methoxyphenyl)benzo[b]thiophen-2-yl)phenol (**3da**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.69 (s, 6H, OC*H*$_3$), 3.76 (s, 3H, OC*H*$_3$), 5.54 (s, 1H, O*H*), 6.59 (s, 2H, ArC*H*), 6.91-6.97 (m, 3H, ArC*H*), 7.31-7.37 (m, 3H, ArC*H*), 7.57-7.59 (m, 1H, ArC*H*), 7.84-7.87 (m, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 55.5 (O*C*H$_3$), 56.2 (O*C*H$_3$), 106.6 (Ar*C*H), 113.3 (Ar*C*H), 115.9 (Ar*C*H), 122.1 (Ar*C*H), 123.0 (Ar*C*H), 123.3 (Ar*C*H), 124.58 (Ar*C*H), 124.63 (Ar*C*H), 125.3 (Ar*C*), 129.9 (Ar*C*H), 132.5 (Ar*C*), 134.7 (Ar*C*), 137.5 (Ar*C*), 138.4 (Ar*C*), 139.8 (Ar*C*), 141.1 (Ar*C*), 146.9 (Ar*C*), 160.1 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{23}H_{21}O_4S$ (M+H$^+$), 393.1155; found 393.1145.

*2,6-Dimethoxy-4-(3-(4-methoxyphenyl)benzo[b]thiophen-2-yl)phenol (**3ea**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.69 (s, 6H, OC*H*$_3$), 3.85 (s, 3H, OC*H*$_3$), 5.55 (s, 1H, O*H*), 6.57 (s, 2H, ArC*H*), 6.97 (d, *J* = 8.8 Hz, 2H, ArC*H*), 7.28 (d, *J* = 8.8 Hz, 2H, ArC*H*), 7.32-7.36 (m, 2H, ArC*H*), 7.56-7.58 (m, 1H, ArC*H*), 7.84-7.86 (m, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 55.5 (O*C*H$_3$), 56.2 (O*C*H$_3$), 106.6 (Ar*C*H), 114.4 (Ar*C*H), 122.1 (Ar*C*H), 123.3 (Ar*C*H), 124.5 (Ar*C*H), 124.6 (Ar*C*H), 125.6 (Ar*C*), 128.3 (Ar*C*), 131.7 (Ar*C*H), 132.4 (Ar*C*), 134.6 (Ar*C*), 138.4 (Ar*C*), 139.4 (Ar*C*), 141.4 (Ar*C*), 146.9 (Ar*C*), 159.1 (Ar*C*), ppm. **HRMS** (ESI): Calcd. for $C_{23}H_{19}O_4S$ (M-H$^+$), 391.1010; found 391.1006.

*2,6-Dimethoxy-4-(3-(4-(trifluoromethyl)phenyl)benzo[b]thiophen-2-yl)phenol (**3fa**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.66 (s, 6H, OC*H*$_3$), 5.54 (s, 1H, O*H*), 6.48 (s, 2H, ArC*H*), 7.36-7.40 (m, 2H, ArC*H*), 7.49-7.55 (m, 3H, ArC*H*), 7.70 (d, *J* = 8.0 Hz, 2H, ArC*H*), 7.87-7.89 (m, 1H, ArC*H*) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ = (1 × Ar*C* missing), 56.1 (O*C*H$_3$), 106.7 (Ar*C*H), 122.3 (Ar*C*H), 122.8 (Ar*C*H), 124.3 (q, *J* = 272.0 Hz, *C*F$_3$), 124.8 (Ar*C*), 124.9 (Ar*C*H), 124.9 (Ar*C*H), 125.8 (q, *J* = 3.7 Hz, Ar*C*H), 129.7 (q, *J* = 32.6 Hz, Ar*C*), 131.1 (Ar*C*H), 135.0 (Ar*C*), 138.6 (Ar*C*), 140.1 (Ar*C*), 140.5 (Ar*C*), 141.1 (Ar*C*), 147.0 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{23}H_{16}F_3O_3S$ (M-H$^+$), 429.0767; found 429.0770.

*4-(3,5-Dimethylbenzo[b]thiophen-2-yl)-2,6-dimethoxyphenol (**3ga**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.45 (s, 3H, CH_3), 2.51 (s, 3H, CH_3), 3.94 (s, 6H, OCH_3), 5.62 (s, 1H, O*H*), 6.76 (s, 2H, ArC*H*), 7.18 (d, *J* = 8.0 Hz, 1H, ArC*H*), 7.50 (s, 1H, ArC*H*), 7.69 (d, *J* = 8.0 Hz, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.8 (*C*H_3), 21.7 (*C*H_3), 56.5 (O*C*H_3), 106.8 (Ar*C*H), 121.8 (Ar*C*H), 122.2 (Ar*C*H), 126.0 (Ar*C*H), 126.1 (Ar*C*), 126.8 (Ar*C*), 134.0 (Ar*C*) 134.8 (Ar*C*), 135.8 (Ar*C*), 138.5 (Ar*C*), 141.6 (Ar*C*), 147.1 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{18}H_{17}O_3S$ (M-H$^+$), 313.0904; found 313.0900.

*4-(5-Chloro-3-methylbenzo[b]thiophen-2-yl)-2,6-dimethoxyphenol (**3ha**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.43 (s, 3H, CH_3), 3.94 (s, 6H, OCH_3), 5.63 (s, 1H, O*H*), 6.74 (s, 2H, ArC*H*), 7.30 (d, *J* = 8.4 Hz, 1H, ArC*H*), 7.67 (s, 1H, ArC*H*), 7.71 (d, *J* = 8.4 Hz, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = (1 × Ar*C* missing), 12.8 (*C*H_3), 56.6 (O*C*H_3), 106.8 (Ar*C*H), 121.8 (Ar*C*H), 123.2 (Ar*C*H), 124.7 (Ar*C*H), 125.4 (Ar*C*), 126.5 (Ar*C*), 130.7 (Ar*C*), 135.2 (Ar*C*), 136.8 (Ar*C*), 140.6 (Ar*C*), 147.2 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{17}H_{14}ClO_3S$ (M-H$^+$), 333.0358; found 333.0352.

*2,6-Dimethoxy-4-(2-methylbenzo[b]thiophen-3-yl)phenol (**3a'a**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.51 (s, 3H, CH_3), 3.91 (s, 6H, OCH_3), 5.62 (s, 1H, O*H*), 6.61 (s, 2H, ArC*H*), 7.29-7.32 (m, 2H, ArC*H*), 7.52-7.54 (m, 1H, ArC*H*), 7.78-7.80 (m, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 14.7 (*C*H_3), 56.5 (O*C*H_3), 106.9 (Ar*C*H), 122.1 (Ar*C*H), 122.5 (Ar*C*H), 123.9 (Ar*C*H), 124.3 (Ar*C*H), 126.4 (Ar*C*), 134.1 (Ar*C*), 134.2 (Ar*C*), 136.0 (Ar*C*), 138.2 (Ar*C*), 140.6 (Ar*C*), 147.2 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{17}H_{15}O_3S$ (M-H$^+$), 299.0736; found 299.0745.

*2,6-Dimethoxy-4-(2-phenylbenzo[b]thiophen-3-yl)phenol (**3b'a**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.74 (s, 6H, OCH_3), 5.57 (s, 1H, O*H*), 6.54 (s, 2H, ArC*H*), 7.24-7.28 (m, 3H, ArC*H*), 7.33-7.37 (m, 4H, ArC*H*), 7.65-7.67 (m, 1H, ArC*H*), 7.85-7.88 (m, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 56.4 (O*C*H_3), 107.3 (Ar*C*H), 122.3 (Ar*C*H), 123.4 (Ar*C*H), 124.6 (Ar*C*H), 124.7 (Ar*C*H), 126.5 (Ar*C*), 127.8 (Ar*C*H), 128.5 (Ar*C*H), 129.6 (Ar*C*H), 133.3 (Ar*C*), 134.3 (Ar*C*), 134.4 (Ar*C*), 138.8 (Ar*C*), 139.4 (Ar*C*), 141.0 (Ar*C*), 147.4 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{22}H_{19}O_3S$ (M+H$^+$), 363.1049; found 363.1048.

*5'-(3-Methylbenzo[b]thiophen-2-yl)-[1,1':3',1''-terphenyl]-2'-ol (**3ab**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.52 (s, 3H, CH_3), 5.53 (s, 1H, O*H*), 7.32-7.36 (m, 1H, ArC*H*), 7.39-7.44 (m, 3H, ArC*H*), 7.48 (s, 2H, ArC*H*), 7.49-7.53 (m, 4H, ArC*H*), 7.60-7.63 (m, 4H, ArC*H*), 7.72 (d, *J* = 7.6 Hz, 1H, ArC*H*), 7.82 (d, *J* = 8.0 Hz, 1H, ArC*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = (3 × Ar*C* missing), 13.0 (*C*H_3), 122.2 (Ar*C*H), 122.3 (Ar*C*H), 124.3 (Ar*C*H), 124.3 (Ar*C*H), 127.2 (Ar*C*), 127.4 (Ar*C*), 128.1 (Ar*C*H), 129.1 (Ar*C*H), 129.5 (Ar*C*H), 131.2, (Ar*C*H), 137.2 (Ar*C*), 138.8 (Ar*C*), 149.3 (Ar*C*) ppm.

*5-Fluoro-2-methoxy-4-(3-methylbenzo[b]thiophen-2-yl)phenol (**3ac**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.33 (d, *J* = 1.9 Hz, 3H, CH_3), 3.91 (s, 3H, OCH_3), 5.83 (s, 1H, O*H*), 6.81 (d, *J* = 10.1 Hz, 1H, ArC*H*), 6.88 (d, *J* = 6.6 Hz, 1H, ArC*H*), 7.35 (ddd, *J* = 8.3, 7.3, 1.3 Hz, 1H, ArC*H*), 7.41 (ddd, *J* = 8.0, 7.2, 1.2 Hz, 1H, ArC*H*), 7.73 (d, *J* = 7.5 Hz, 1H, ArC*H*), 7.83 (d, *J* = 7.7 Hz, 1H, ArC*H*), ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.9 (d, *J* = 3.6 Hz, *C*H_3), 56.6 (O*C*H_3), 103.3 (d, *J* = 28.0 Hz, Ar*C*H), 112.7 (d, *J* = 17.4 Hz, Ar*C*), 113.4 (d, *J* = 4.2 Hz, Ar*C*H), 122.2 (Ar*C*H), 122.3 (Ar*C*H), 124.3 (Ar*C*H), 124.5 (Ar*C*H), 130.2 (Ar*C*), 131.3 (Ar*C*), 139.5 (Ar*C*), 140.7 (Ar*C*), 143.0 (d, *J* = 2.4 Hz, Ar*C*), 147.0 (d, *J* = 12.4 Hz, Ar*C*), 154.6 (d, *J* = 242.0 Hz, Ar*C*F) ppm.

*2-Chloro-4-methoxy-6-(3-methylbenzo[b]thiophen-2-yl)phenol (**3ad**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.34 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 5.39 (s, 1H, O*H*), 6.84 (d, *J* = 2.8 Hz, 1H, ArC*H*), 7.00 (d, *J* = 2.8 Hz, 1H, ArC*H*), 7.37-7.46 (m, 2H, ArC*H*), 7.76 (d, *J* = 8.0 Hz, 1H, ArC*H*), 7.85 (d, *J* = 8.0 Hz, 1H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = (1 × Ar*C* missing), 12.8 (*C*H_3), 56.1 (O*C*H_3), 115.6 (Ar*C*H), 116.4 (Ar*C*H), 121.0 (Ar*C*), 122.40 (Ar*C*H), 122.43 (Ar*C*H), 124.4 (Ar*C*H), 124.9 (Ar*C*H), 131.0 (Ar*C*), 131.7 (Ar*C*), 139.8 (Ar*C*), 140.5 (Ar*C*), 143.7 (Ar*C*), 153.0 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{16}H_{12}ClO_2S$ (M-H$^+$), 303.0252; found 303.0248.

*4-Methoxy-2,6-bis(3-methylbenzo[b]thiophen-2-yl)phenol (**4**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.39 (s, 6H, CH_3), 3.90 (s, 3H, OCH_3), 5.23 (s, 1H, O*H*), 7.00 (s, 2H, ArC*H*), 7.37-7.46 (m, 4H, ArC*H*), 7.77 (d, *J* = 7.6 Hz, 2H, ArC*H*), 7.86 (d, *J* = 8.0 Hz, 2H, ArC*H*) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.9 (*C*H_3), 56.0 (O*C*H_3), 117.9 (Ar*C*H), 121.9 (Ar*C*), 122.40 (Ar*C*H), 122.42 (Ar*C*H), 124.4 (Ar*C*H), 124.8 (Ar*C*H), 130.9 (Ar*C*), 132.4 (Ar*C*), 139.9 (Ar*C*), 140.6 (Ar*C*), 145.5 (Ar*C*), 152.7 (Ar*C*) ppm. **HRMS** (ESI): Calcd. for $C_{25}H_{21}O_2S_2$ (M+H$^+$), 417.0977; found 417.0971.

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Supplementary Material

Supplementary material, including NMR spectra and crystallographic data, have been provided as a separate electronic file.

Declaration of interests

☐**X** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: