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A cyclization–carbonylation–cyclization coupling reaction of (*ortho*-alkynyl phenyl) (methoxymethyl) sulfides with the palladium(II)-bisoxazoline catalyst†

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A cyclization–carbonylation–cyclization coupling reaction (CCC-coupling reaction) of (*o*-alkynylphenyl) (methoxymethyl) sulfides, catalyzed by (box)Pd^{II} complexes, afforded symmetrical ketones bearing two benzo[*b*]thiophene groups in good to excellent yields. This method is applicable to a broad range of substrates.

Introduction

Benzo[*b*]thiophenes have been recognized to be an important class of *S*-heterocycles in pharmaceutical sciences.[1] They exhibit various interesting biological properties, such as anti-tumor,[2a] antipsychotic,[2b] anti-inflammatory,[2c] antiallergic,[2d] and antimicrobial activities[2e] and the inhibition of tubulin polymerization[2f] (Fig. 1). Diarylketones are also frequently found in natural products and pharmaceuticals,[3] *e.g.*, suprofen (non-steroidal anti-inflammatory), raloxifene (selective estrogen receptor modulator used for the treatment of osteoporosis), benzbromarone (antipodagric) and amiodarone (antiarrhythmic). A variety of heterocycles can be synthesized by transition-metal-catalyzed cyclization of unsaturated systems.[4] Among these, *ortho*-alkynyl phenyl sulfides are good precursors for the synthesis of benzo[*b*]thiophenes.[5]

Recently, we reported that the cyclization–carbonylation–cyclization coupling reaction (CCC-coupling reaction) of propargylic compounds using palladium(II)-bisoxazoline (box) complexes afforded symmetrical ketones bearing two oxazoles, cyclic orthoesters, oxabicyclic groups, quinolines, benzofurans, oxazolines and pyrazoles (Scheme 1).[6] The CCC-coupling is a two-component (three molecules) coupling reaction based on double intramolecular cyclization of propargylic compounds bearing nucleophiles in conjunction with incorporation of carbon monoxide. Two C–X bonds and two C–C bonds are formed in one-step reactions. In this transformation, the box ligand plays an important role in the coordination of a second molecule in intermediate **A**, and methanolysis of the acyl palladium should be suppressed by coordination of this second molecule. To extend the generality of the CCC-coupling reaction, we investigated the (box)Pd^{II}-catalyzed carbonylation reaction of (*o*-alkynylphenyl) (methoxymethyl) sulfides **1** (Tables 1 and 2).

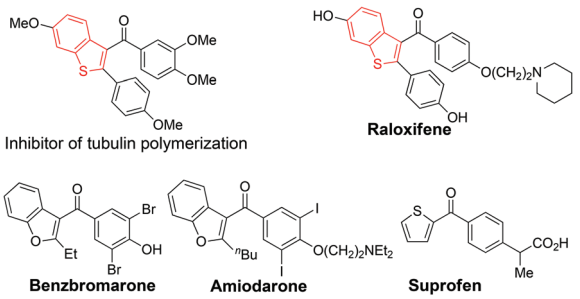
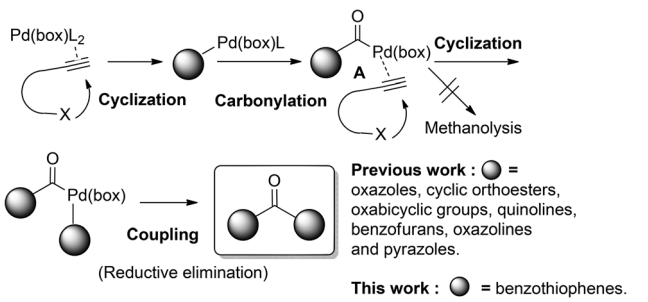


Fig. 1 Structures of biologically active benzo[*b*]thiophenes and diarylketones.



Scheme 1 Cyclization–carbonylation–cyclization-coupling reaction (CCC-coupling reaction) of propargylic compounds.

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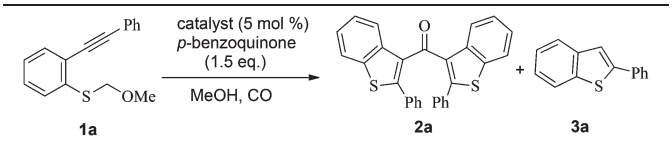
Table 1 Optimization of the CCC-coupling reaction of **1a**

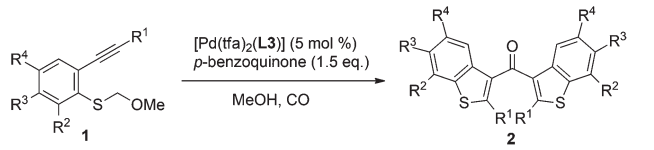


1a 2a 3a

Entry	Catalyst	Temp (°C), time (h)	Yield of **2a** (%)	Yield of **3a** (%)
1	$Pd(tfa)_2$	−20 to −10, 45	49	11
2	$[PdCl_2(2,2'\text{-bipy})]$[a]	−20 to −10, 45	41	18
3[c]	$[Pd(tfa)_2(2,2'\text{-bipy})]$[b]	−20 to −10, 24	—	28
4[c]	5% Pd–C	−30, 48	—	—
5	$Pd(tfa)_2$/**L1**[d]	−30, 26	86	Trace
6	$[Pd(tfa)_2(\mathbf{L2})]$[b]	−30 to −10, 19	85	10
7	$[Pd(tfa)_2(\mathbf{L3})]$[b]	−30 to −10, 31	Quant.	—
8	$Pd(tfa)_2$/**L4**[d]	−20 to −10, 48	77	2
9	$Pd(tfa)_2$/**L5**[d]	−20 to −10, 48	70	2
10[e]	$[Pd(OAc)_2(\mathbf{L3})]$[b]	−20 to −10, 48	58	7
11	$[PdCl_2(\mathbf{L3})]$[b]	−30 to −10, 72	86	Trace

[a] Commercially available. [b] The isolated complex was employed. [c] Recovery 57–93%. [d] $Pd(tfa)_2$ 5 mol% and **L1** 7.5 mol%. [e] Recovery 20%.

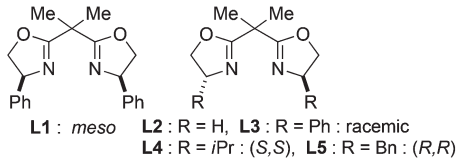
Table 2 Substrate scope of the CCC-coupling reaction



Entry	R^1	R^2	R^3	R^4	Temp (°C), time (h)	Yield (%)
1	Ph	H	H	H	−30 to −10, 31	**2a:** quant.
2	4-MePh	H	H	H	−30 to −10, 72	**2b:** 82
3	4-MeOPh	H	H	H	−40 to −30, 31	**2c:** 88
4	4-CF_3Ph	H	H	H	−40 to −20, 78	**2d:** 88
5	4-FPh	H	H	H	−30 to −10, 72	**2e:** 84
6	4-BrPh	H	H	H	−35 to −25, 114	**2f:** 89
7	4-ClPh	H	H	H	−30 to −10, 72	**2g:** 84
8	3-Thienyl	H	H	H	−40 to −20, 68	**2h:** 84
9	Phenethyl	H	H	H	−30, 42	**2i:** 95
10	Octyl	H	H	H	−30, 24	**2j:** 80
11	Cyclopropyl	H	H	H	−30, 48	**2k:** 86
12	$HO(CH_2)_9$	H	H	H	−30 to −20, 72	**2l:** 87
13	H	H	H	H	−20 to rt, 72	**2m:** 80
14	Ph	H	H	Cl	−30 to −20, 72	**2n:** 83
15	4-*t*BuPh	H	H	Cl	−30 to −20, 40	**2o:** 86
16	Ph	H	H	Me	−30, 24	**2p:** 99
17	Ph	Me	H	Me	−30 to −20, 44	**2q:** 82
18	Ph	H	MeO	H	−30, 74	**2r:** 75
19	4-MeOPh	H	MeO	H	−30 to −20, 144	**2s:** 97
20	3-HOPh	H	MeO	H	−30, 144	**2t:** 77
21	3,5-$(MeO)_2$Ph	H	MeO	H	−30 to −20, 31	**2u:** 78

Results and discussion

The (*o*-alkynylphenyl) (methoxymethyl) sulfides **1** were prepared from known *o*-iodoanilines by modification of a published procedure.[8] Initially, we selected **1a** as a standard substrate to search for potential catalysts (Table 1). The reaction of **1a** with $Pd(tfa)_2$ (5 mol%) and *p*-benzoquinone

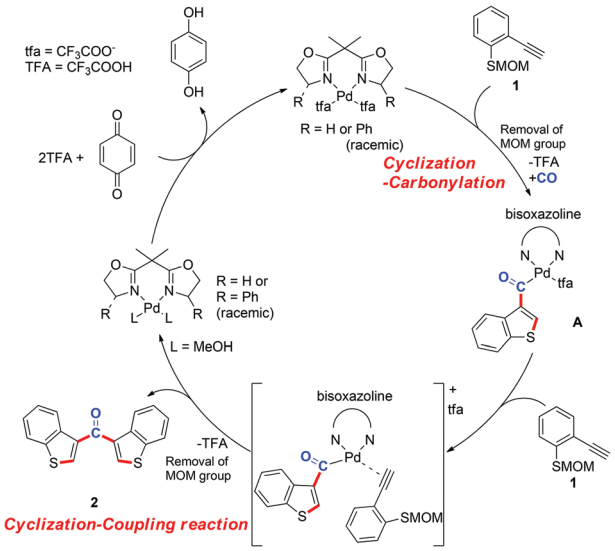


L1 : *meso* **L2** : R = H, **L3** : R = Ph : racemic
L4 : R = *i*Pr : (*S*,*S*), **L5** : R = Bn : (*R*,*R*)

Fig. 2 Ligands for Table 1.

(1.5 equiv.) in methanol under a carbon monoxide atmosphere (balloon) generated the dimeric ketone **2a** in 49% yield along with 11% yield of **3a** (Table 1, entry 1). These products were easily separated by silica gel chromatography. The use of 2,2′-bipyridine complexes also gave poor results (Table 1, entries 2 and 3). The phosphine complexes $Pd(PPh_3)_4$, $[PdCl_2(PPh_3)_2]$ and Pd–C (Table 1, entry 4) did not show catalytic activity. Next, an attempt was made to use the box ligands **L1–L5** (Table 1, entries 5–9, Fig. 2). In our previous research,[6,7] substituents at the C4 position of the box ligands played an important role in promoting the attempted reactions. In this case, however, all box ligands exhibited moderate to good activity. Among them, (±)-Phbox ligand **L3** gave the best result (Table 1, entry 7). In terms of the palladium counteranion, switching from trifluoroacetate to acetate caused a decrease in the yields (Table 1, entry 10). The Lewis acidity of palladium(II) is expected to decrease with increasing nucleophilicity of its counteranion.[9] Chloride showed a moderate catalytic activity (Table 1, entry 11). Furthermore, THF and CH_2Cl_2 were not suitable as solvents, as the reaction did not proceed when they were used.

Having elucidated the optimum conditions for the reaction, we then employed a variety of (*o*-alkynylphenyl) (methoxymethyl) sulfides **1** in the CCC-coupling reaction (Table 2). First, the reaction of substrates derived from (*o*-iodophenyl) (methoxymethyl) sulfides and ArC≡CH (R^1 = Ar, R^2–R^4 = H) was investigated (Table 2, entries 1–8). The substrates **1b–1d** bearing both electron-donating and electron-withdrawing substituents gave good results, similar to that of the parent substrate **1a** (Table 2, entries 2–4). Three kinds of halogen substituents (F, Cl, and Br) on the phenyl ring and a thiophene ring in the alkyne terminus were tolerated under the reaction conditions (Table 2, entries 5–8). Replacement of the aryl groups at the alkyne terminus with alkyl groups also led to the desired **2i–2k** in good yield (Table 2, entries 9–11). A free hydroxyl group in the alkyne terminus was also tolerated under the reaction conditions, providing **2l** in 87% yield (Table 2, entry 12). It is noteworthy that the terminal acetylene **1m** was transformed to the corresponding ketone **2m** in 80% yield (Table 2, entry 13). To further broaden the substrate scope of the CCC-coupling reaction, the reactions of substrates bearing R^2–R^4 substituents were investigated (Table 2, entries 14–21). For substrates **1n–1q** bearing a methyl group or Cl substituents in an aromatic moiety, the reaction proceeded well (Table 2, entries 14–17). The substrates **1r–1u** bearing electron-donating groups afforded slightly lower yields (75–78%) of the products except in the case of **1s** (Table 2, entries 18–21).



Scheme 2 A plausible mechanism for the cyclization–carbonylation–cyclization-coupling reaction (CCC-coupling reaction) of (*o*-alkynylphenyl) (methoxymethyl) sulfides **1**.

A plausible mechanism for the reaction of **1** is shown in Scheme 2. A nucleophilic attack by the sulfur atom at the electrophilically activated triple bond was followed by CO insertion to produce the acyl palladium intermediate **A**. The methoxymethyl group may be removed by acetal exchange (or hydrolysis) during the formation of intermediate **A**. Coordination of the triple bond of a second molecule induces the second cyclization, and reductive elimination then leads to the formation of a ketone bearing two heterocyclic groups. We believe that the box ligand enhances the π-electrophilicity of palladium(II),[7] and thus promotes coordination of the second triple bond to the acyl palladium intermediate **A**, leading to the dimerization reaction.

Conclusions

In conclusion, we carried out cyclization–carbonylation–cyclization coupling reactions (CCC-coupling reactions) of (*o*-alkynylphenyl) (methoxymethyl) sulfides **1** catalyzed by (box)Pd^{II} complexes. Symmetrical ketones possessing two benzo[*b*]thiophene groups were obtained in good to excellent yields. The reaction was general for a wide range of (*o*-alkynylphenyl) (methoxymethyl) sulfides **1**. We are currently investigating additional cascade reactions based on the cyclization–carbonylation–cyclization strategy presented here for the synthesis of other types of ketones containing two heterocyclic groups.

Experimental section

General information

See ESI† for general experimental details as well as procedures for the preparation and characterization of all precursors and products.

Preparation of box-palladium complexes

The box ligands **L1–L3** and palladium complexes [Pd(tfa)$_2$(2,2′-bipy)], [Pd(tfa)$_2$(**L2**)], [Pd(tfa)$_2$(**L3**)] and [$PdCl_2$(**L3**)] were prepared according to a literature method.[6a,d,10]

General procedure for the CCC-coupling reaction of (*o*-alkynylphenyl) (methoxymethyl) sulfides 1. A 30 mL two-necked round-bottom flask containing a magnetic stirring bar, (*o*-alkynylphenyl) (methoxymethyl) sulfides **1** (0.4 mmol), *p*-benzoquinone (65 mg, 0.6 mmol) and MeOH (3 mL) was fitted with a rubber septum and a three-way stopcock connected to a balloon filled with carbon monoxide. The apparatus was purged with carbon monoxide by pump-filling *via* the three-way stopcock. A MeOH (1 mL) suspension of [Pd(tfa)$_2$(**L3**)] (13.3 mg, 0.02 mmol) was added to the stirred solution *via* a syringe at an appropriate temperature. The remaining catalyst was washed in MeOH (1 mL) twice, and stirred for the period of time. In most cases, the dimeric ketones precipitated from the reaction mixture. The resulting precipitate was collected by filtration and washed with cold MeOH (1.5 mL × 2) to yield dimeric ketones **2**. As small amounts of **2** (and **3a**, see Table 1) still remained in the filtrate, the filtrate was diluted with CH_2Cl_2 (50 mL) and washed with 5% NaOH (40 mL). The aqueous layer was extracted with CH_2Cl_2 (25 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel. The fraction eluted with hexane–EtOAc (100/1) afforded small amounts of dimeric ketones **2** (and monomeric ester **3a** (only hexane)).

Bis(2-phenylbenzo[*b*]thiophen-3-yl)methanone 2a. 100% Yield (86.4 mg), white solid, mp 193–195 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86–6.90 (4H, m), 6.99–7.04 (6H, m), 7.36 (2H, dt, J = 1.2, 8.0 Hz), 7.51 (2H, dt, J = 1.2, 8.0 Hz), 7.65 (2H, br-d, J = 8.0 Hz), 8.33 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.4 (2C), 123.8 (2C), 125.0 (2C), 125.6 (2C), 127.5 (4C), 128.5 (2C), 129.2 (4C), 132.6 (2C), 132.9 (2C), 138.4 (2C), 140.1 (2C), 150.8 (2C), 189.4; IR (KBr) 1633, 1458, 1432, 751, 691 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{29}H_{18}OS_2$ 446.0799, found 446.0801.

2-Phenylbenzo[*b*]thiophene (**3a**) was a known compound.[11]

Bis[2-(4-methylphenyl)benzo[*b*]thiophen-3-yl]methanone 2b. 82% Yield (79.5 mg), white solid, mp 227 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.12 (6H, s), 6.66–6.68 (4H, m), 6.87–6.90 (4H, m), 7.34 (2H, dt, J = 1.2, 8.0 Hz), 7.49 (2H, dt, J = 1.2, 8.0 Hz), 7.63 (2H, br-d, J = 8.0 Hz), 8.28 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1 (2C), 121.3 (2C), 123.7 (2C), 124.7 (2C), 125.4 (2C), 128.2 (4C), 129.0 (4C), 129.8 (2C), 132.5 (2C), 138.3 (2C), 138.5 (2C), 140.1 (2C), 150.9 (2C), 189.6; IR (KBr) 1643, 1531, 676 cm^{-1}; HRMS-EI: m/z: [M^+] calcd for $C_{31}H_{22}OS_2$ 474.1112, found 474.1112.

Bis[2-(4-methoxyphenyl)benzo[*b*]thiophen-3-yl]methanone 2c. 88% Yield (89.2 mg), brown solid, mp 198–201 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.58 (6H, s), 6.35–6.39 (4H, m), 6.90–6.94 (4H, m), 7.34 (2H, dt, J = 1.2, 8.0 Hz), 7.49 (2H, dt, J = 1.2, 8.0 Hz), 7.63 (2H, br-d, J = 8.0 Hz), 8.30 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.2 (2C), 113.0 (4C),

121.3 (2C), 123.6 (2C), 124.7 (2C), 125.2 (2C), 125.5 (2C), 130.5 (4C), 132.0 (2C), 138.3 (2C), 140.3 (2C), 150.8 (2C), 159.8 (2C), 189.7; IR (KBr) 1631, 1604, 1458, 1257, 1180, 1086 cm^{-1}; HRMS-EI: *m*/*z*: [M^+] calcd for $C_{31}H_{22}O_3S_2$ 506.1011, found 506.1011.

Bis[2-(4-trifluoromethylphenyl)benzo[*b*]thiophen-3-yl]-methanone 2d. 88% Yield (102.5 mg), white solid, mp 233–235 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10–7.15 (8H, m), 7.43 (2H, dt, J = 0.8, 8.0 Hz), 7.56 (2H, dt, J = 0.8, 8.0 Hz), 7.69 (2H, br-d, J = 8.0 Hz), 8.29 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.7 (2C), 123.6 (2C, q, $^1J_{C-F}$ = 270.6 Hz), 123.8 (2C), 124.5 (4C, q, $^3J_{C-F}$ = 3.9 Hz), 125.8 (2C), 126.0 (2C), 129.3 (4C), 130.4 (2C, q, $^2J_{C-F}$ = 32.4 Hz), 134.2 (2C), 135.9 (2C), 138.4 (2C), 139.6 (2C), 148.5 (2C), 188.7; IR (KBr) 1646, 1327, 1156, 1123, 1068 cm^{-1}; HRMS-EI: *m*/*z*: [M^+] calcd for $C_{31}H_{16}OF_6S_2$ 582.0547, found 582.0547.

Bis[2-(4-fluorophenyl)benzo[*b*]thiophen-3-yl]methanone 2e. 84% Yield (81.0 mg), white solid, mp 226–227 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56–6.62 (4H, m), 6.95–7.00 (4H, m), 7.39 (2H, br-d, J = 1.2, 8.0 Hz), 7.52 (2H, dt, J = 1.2, 8.0 Hz), 7.69 (2H, br-d, J = 8.0 Hz), 8.28 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.7 (4C, d, $^2J_{C-F}$ = 21.9 Hz), 121.6 (2C), 123.7 (2C), 125.3 (2C), 125.8 (2C), 128.7 (2C, d, $^4J_{C-F}$ = 2.9 Hz), 130.8 (4C, d, $^3J_{C-F}$ = 8.6 Hz), 132.8 (2C), 138.2 (2C), 139.8 (2C), 149.4 (2C), 162.7 (2C, d, $^1J_{C-F}$ = 248.8 Hz), 189.0; IR (KBr) 1630, 1490, 1457, 1232 cm^{-1}; HRMS-ESI$^+$ *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{16}F_2NaOS_2$ 505.0508, found 505.0536.

Bis[2-(4-bromophenyl)benzo[*b*]thiophen-3-yl]methanone 2f. 89% Yield (107.5 mg), yellow solid, mp 268–269 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85–6.88 (4H, m), 7.00–7.04 (4H, m), 7.42 (2H, dt J = 1.2, 8.0 Hz), 7.53 (2H, dt, J = 1.2, 8.0 Hz), 7.72 (2H, br-d, J = 8.0 Hz), 8.26 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.7 (2C), 123.1 (2C), 123.8 (2C), 125.5 (2C), 125.9 (2C), 130.4 (4C), 130.8 (4C), 131.4 (2C), 133.1 (2C), 138.3 (2C), 139.8 (2C), 149.2 (2C), 188.8; IR (KBr) 1654, 1627, 465 cm^{-1}; HRMS-EI: *m*/*z* [M^+] calcd for $C_{29}H_{16}Br_2OS_2$ 601.9010, found 601.9008.

Bis[2-(4-chlorophenyl)benzo[*b*]thiophen-3-yl]methanone 2g. 84% Yield (86.7 mg), yellow solid, mp 241–242 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85–6.88 (4H, m), 6.91–6.95 (4H, m), 7.41 (2H, dt, J = 1.2, 8.0 Hz), 7.53 (2H, dt, J = 1.2, 8.4 Hz), 7.71 (2H, br-d, J = 8.4 Hz), 8.27 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.7 (2C), 123.8 (2C), 125.5 (2C), 125.9 (2C), 127.8 (4C), 130.2 (4C), 131.0 (2C), 133.1 (2C), 134.8 (2C), 138.3 (2C), 139.8 (2C), 149.2 (2C), 188.8; IR (KBr) 1628, 1431, 1090, 776 cm^{-1}; HRMS-EI: *m*/*z* [M^+] calcd for $C_{29}H_{16}Cl_2OS_2$ 514.0020, found 514.0017.

Bis[2-(thiophen-3-yl)benzo[*b*]thiophen-3-yl]methanone 2h. 84% Yield (77.0 mg), dark brown solid, mp 179–181 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.74 (2H, dd, J = 1.2, 4.8 Hz), 6.97 (2H, dd, J = 2.8, 4.8 Hz), 7.05 (2H, dd, J = 1.2, 2.8 Hz), 7.40 (2H, dt, J = 0.8, 8.0 Hz), 7.48 (2H, dt, J = 0.8, 8.0 Hz), 7.74 (2H, br-d, J = 8.0 Hz), 8.19 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 121.9 (2C), 124.1 (2C), 125.5 (2C), 125.6 (2C), 125.7 (2C), 126.0 (2C), 128.5 (2C), 132.6 (2C), 133.5 (2C), 138.6 (2C), 139.9 (2C), 145.6 (2C), 188.7; IR (KBr) 1631, 1458, 1191, 840, 770, 755 cm^{-1}; HRMS-EI *m*/*z* [M^+] calcd for $C_{25}H_{14}OS_4$ 457.9928, found 457.9929.

Bis[2-(2-phenylethyl)benzo[*b*]thiophen-3-yl]methanone 2i. 95% Yield (95.5 mg), yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.83–2.93 (4H, m), 3.04–3.12 (4H, m), 6.92–6.95 (4H, m), 7.10–7.19 (6H, m), 7.24 (2H, dt, J = 1.2, 8.0 Hz), 7.31 (2H, dt, J = 1.2, 7.2 Hz), 7.57 (2H, br-d, J = 8.0 Hz), 7.80 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.9 (2C), 37.9 (2C), 122.0 (2C), 123.3 (2C), 124.7 (2C), 125.2 (2C), 126.2 (2C), 128.31 (4C), 128.33 (2C), 128.4 (4C), 133.9 (2C), 138.1 (2C), 140.3 (2C), 152.7 (2C), 188.3; IR (KBr) 2923, 1636, 1455, 1432, 1188, 745, 698 cm^{-1}; HRMS-EI: *m*/*z* [M^+] calcd for $C_{33}H_{26}OS_2$ 502.1425, found 502.1425.

Bis(2-octylbenzo[*b*]thiophen-3-yl)methanone 2j. 80% Yield (83.0 mg), pale yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (6H, t, J = 7.5 Hz), 1.13–1.26 (20H, m), 1.59–1.60 (4H, m), 2.78 (4H, t, J = 7.5 Hz), 7.23–7.31 (4H, m), 7.64 (2H, br-d, J = 7.5 Hz), 7.78 (2H, br-d, J = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 (2C), 22.6 (2C), 29.1 (2C), 29.1 (2C), 29.4 (2C), 29.7 (2C), 31.8 (2C), 32.0 (2C), 121.9 (2C), 123.1 (2C), 124.5 (2C), 125.1 (2C), 133.6 (2C), 137.7 (2C), 138.4 (2C), 154.1 (2C), 188.7; IR (KBr): 2924, 2853, 1637, 1457, 1433, 1188 cm^{-1}; HRMS-EI: *m*/*z*: [M^+] calcd for $C_{33}H_{42}OS_2$ 518.2677, found 518.2675.

Bis(2-cyclopropylbenzo[*b*]thiophen-3-yl)methanone 2k. 86% Yield (64.4 mg), white solid, mp 260–262 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82–0.92 (8H, m), 2.13–2.20 (2H, m), 7.27–7.33 (4H, m), 7.70–7.74 (2H, m), 7.80–7.84 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.9 (4C), 12.0 (2C), 121.8 (2C), 123.0 (2C), 124.5 (2C), 125.2 (2C), 134.7 (2C), 136.3 (2C), 138.8 (2C), 157.2 (2C), 188.6; IR (KBr) 2923, 1629, 1515, 1447, 1358, 734 cm^{-1}; HRMS-EI *m*/*z* [M^+] calcd for $C_{23}H_{18}OS_2$ 374.0799, found 374.0794.

Bis[(2-(9-hydroxynonyl)benzo[*b*]thiophen-3-yl]methanone 2l. 87% Yield (100.6 mg), yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15–1.32 (22H, m), 1.49–1.60 (6H, m), 1.77 (2H, br-s), 2.79 (4H, t, J = 7.8 Hz), 3.60 (4H, t, J = 6.6 Hz), 7.23–7.32 (4H, m), 7.63 (2H, br-d, J = 7.2 Hz), 7.78 (2H, br-d, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6 (2C), 29.0 (2C), 29.3 (4C), 29.4 (2C), 29.7 (2C), 31.9 (2C), 32.7 (2C), 63.0 (2C), 121.9 (2C), 123.1 (2C), 124.5 (2C), 125.1 (2C), 133.6 (2C), 137.6 (2C), 138.3 (2C), 154.1 (2C), 188.7; IR (KBr) 3365, 2925, 2853, 1635, 1434, 1065 cm^{-1}; HRMS-EI *m*/*z* [M^+] calcd for $C_{35}H_{46}O_3S_2$ 578.2889, found 578.2888.

Bis(benzo[*b*]thiophen-3-yl)methanone 2m.[12]. 80% Yield (47 mg), white solid, mp 167–168 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.54 (4H, m), 7.91 (2H, br-d, J = 8.0 Hz), 8.08 (2H, s), 8.57 (2H, br-d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 122.4 (2C), 125.0 (2C), 125.7 (2C), 125.7 (2C), 136.4 (2C), 136.8 (2C), 137.3 (2C), 140.2 (2C), 184.9; IR (KBr) 1627, 1189, 1065, 1550, 677 cm^{-1}; HRMS-EI *m*/*z* [M^+] calcd for $C_{17}H_{10}OS_2$ 294.0173, found 294.0175.

Bis(5-chloro-2-phenylbenzo[*b*]thiophen-3-yl)methanone 2n. 83% Yield (85.6 mg), white solid, mp 209–211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.91–6.98 (8H, m), 7.04–7.09 (2H, m), 7.34 (2H, dd, J = 2.0, 8.4 Hz), 7.56 (2H, d, J = 8.4 Hz), 8.34 (2H, d, J = 2.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$) δ = 122.5 (2C), 123.4

(2C), 125.6 (2C), 127.7 (4C), 129.0 (2C), 129.2 (6C), 131.8 (2C), 132.1 (2C), 136.4 (2C), 141.0 (2C), 152.7 (2C), 188.5; IR (KBr) 1622, 1423, 1150, 1071, 747 cm^{-1}; HRMS-EI *m/z*: $[M^+]$ calcd for $C_{29}H_{16}Cl_2OS_2$ 514.0020, found 514.0026.

Bis[2-(4-*tert*-butylphenyl)-5-chlorobenzo[*b*]thiophen-3-yl]-methanone 2o. 86% Yield (108.0 mg), white solid, mp 280–281 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 1.13 (18H, s), 6.89 (8H, s), 7.33 (2H, dd, *J* = 2.0, 8.4 Hz), 7.50 (2H, br-d, *J* = 8.4 Hz), 8.30 (2H, br-d, *J* = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9 (6C), 34.4 (2C), 122.3 (2C), 123.2 (2C), 124.5 (4C), 125.3 (2C), 129.0 (4C), 129.2 (2C), 131.9 (2C), 132.0 (2C), 136.3 (2C), 141.2 (2C), 152.2 (2C), 152.8 (2C), 188.9; IR (KBr) 2957, 1642, 1627, 1549, 1426, 1079, 675 cm^{-1}; HRMS-ESI$^+$ *m/z* $[M + Na]^+$ calcd for $C_{37}H_{32}Cl_2NaOS_2$ 649.1169, found 649.1191.

Bis(5-methyl-2-phenylbenzo[*b*]thiophen-3-yl)methanone 2p. 99% Yield (94.9 mg), brown solid, mp 170–172 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 2.56 (6H, s), 6.86–6.90 (4H, m), 6.96–7.00 (4H, m), 7.00–7.05 (2H, m), 7.19 (2H, br-d, *J* = 8.4 Hz), 7.52 (2H, d, *J* = 8.4 Hz), 8.16 (2H, br-s); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 21.8 (2C), 121.0 (2C), 123.7 (2C), 126.7 (2C), 127.5 (4C), 128.4 (2C), 129.2 (4C), 132.4 (2C), 132.8 (2C), 135.4 (2C), 135.7 (2C), 140.4 (2C), 151.1 (2C), 189.5; IR (KBr) 1636, 1509, 1439, 758, 743, 693 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{31}H_{22}OS_2$ 474.1112, found 474.1112.

Bis(5,7-dimethyl-2-phenylbenzo[*b*]thiophen-3-yl)methanone 2q. 82% Yield (83.1 mg), pale yellow solid, mp 229–231 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 2.40 (6H, s), 2.52 (6H, s), 6.86–6.90 (4H, m), 6.98–7.03 (8H, m), 7.99 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 20.0 (2C), 21.7 (2C), 121.4 (2C), 127.0 (2C), 127.4 (4C), 128.2 (2C), 129.2 (4C), 130.4 (2C), 133.0 (2C), 133.0 (2C), 135.8 (2C), 135.9 (2C), 140.3 (2C), 150.5 (2C), 189.8; IR (KBr) 1614, 1364, 1270, 756, 717, 699 cm^{-1}; HRMS-EI *m/z*: $[M^+]$ calcd for $C_{33}H_{26}OS_2$ 502.1425, found 502.1424.

Bis(6-methoxy-2-phenylbenzo[*b*]thiophen-3-yl)methanone 2r. 75% Yield (76.1 mg), pale yellow solid, mp 224–225 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 3.89 (6H, s), 6.89–6.98 (8H, m), 7.02–7.07 (2H, m), 7.11–7.14 (4H, m), 8.19 (2H, br-d, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 55.6 (2C), 104.0 (2C), 115.2 (2C), 124.6 (2C), 127.5 (4C), 128.3 (2C), 129.2 (4C), 132.4 (2C), 132.7 (2C), 134.3 (2C), 139.9 (2C), 148.4 (2C), 157.7 (2C), 189.4; IR (KBr) 1624, 1601, 1474, 1252, 1052, 744 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{31}H_{22}O_3S_2$ 506.1011, found 506.1009.

Bis[6-methoxy-2-(4-methoxyphenyl)benzo[*b*]thiophen-3-yl]-methanone 2s. 97% Yield (109.9 mg), yellow powder, mp 215–217 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 3.64 (6H, s), 3.88 (6H, s), 6.41–6.44 (4H, m), 6.88–6.92 (4H, m), 7.09–7.12 (4H, m), 8.15–8.17 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 55.3 (2C), 55.6 (2C), 104.0 (2C), 113.0 (4C), 115.0 (2C), 124.4 (2C), 125.4 (2C), 130.4 (4C), 131.6 (2C), 134.3 (2C), 139.6 (2C), 148.5 (2C), 157.5 (2C), 159.6 (2C), 189.6; IR (KBr) 3855, 1604, 1475, 1249, 1056 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{33}H_{26}O_5S_2$ 566.1222, found 566.1222.

Bis[2-(3-hydroxyphenyl)-6-methoxybenzo[*b*]thiophen-3-yl]-methanone 2t. 77% Yield (83.1 mg), yellow powder, mp 295–296 °C; ^1H NMR (400 MHz, DMSO-d_6) δ = 3.83 (6H, s), 6.36–6.50 (6H, m), 6.66 (2H, t, *J* = 8.0 Hz), 7.11 (2H, dd, *J* = 2.4, 8.8 Hz), 7.43 (2H, d, *J* = 2.4 Hz), 7.97 (2H, d, *J* = 8.8 Hz), 9.34 (2H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 55.5 (2C), 104.4 (2C), 115.2 (2C), 115.3 (2C), 115.5 (2C), 120.0 (2C), 124.1 (2C), 128.5 (2C), 132.1 (2C), 133.4 (2C), 133.5 (2C), 139.1 (2C), 147.4 (2C), 156.7 (2C), 157.2 (2C), 188.7; IR (KBr) 3372, 1602, 1592, 1238, 1060, 771 cm^{-1}; HRMS-EI: *m/z* $[M^+]$ calcd for $C_{31}H_{22}O_5S_2$ 538.0909, found 538.0907.

Bis[2-(3,5-dimethoxyphenyl)-6-methoxybenzo[*b*]thiophen-3-yl]methanone 2u. 78% Yield (97.7 mg), yellow solid, mp 117–118 °C; ^1H NMR (400 MHz, $CDCl_3$) δ = 3.46 (12H, s), 3.89 (6H, s), 6.12 (4H, d, *J* = 2.4 Hz), 6.19 (2H, t, *J* = 2.4 Hz), 7.11 (2H, dd, *J* = 2.4, 8.8 Hz), 7.16 (2H, d, *J* = 2.4 Hz), 8.27 (2H, d, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 55.0 (4C), 55.6 (2C), 101.3 (2C), 104.1 (2C), 107.4 (4C), 115.3 (2C), 125.0 (2C), 131.9 (2C), 134.1 (2C), 134.5 (2C), 139.8 (2C), 148.8 (2C), 157.8 (2C), 159.8 (4C), 188.9; IR (KBr) 1618, 1597, 1457, 1271, 1203, 1152, 1066 cm^{-1}; HRMS-ESI$^+$ *m/z* $[M + Na]^+$ calcd for $C_{35}H_{30}NaO_7S_2$ 649.1331, found 649.1340.

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