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SYNTHESIS OF BIS(BENZO[*b*]THIOPHENYL)METHANES BY GOLD-CATALYZED DOUBLE CARBOTHIOLATION†

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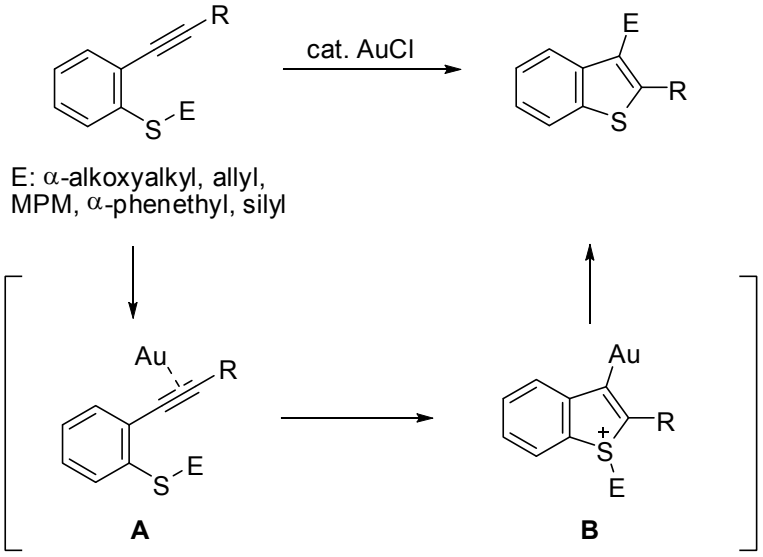
†Dedicated to Professor Dr. Albert Eschenmoser on the occasion of his 85th birthday.

Abstract – Gold-catalyzed double cyclization of bis(2-alkynylphenylthio)acetals (**1**) produced bis(benzo[*b*]thiophen-3-yl)methanes (**2**) in good to excellent yields with high catalyst turnover number. For example, the reaction of (phenylmethylene)bis((2-(phenylethynyl)phenyl)sulfane) (**1b**) in the presence of 1 mol% of AuCl in toluene at 25 °C for 1 hour gave 3,3'-(phenylmethylene)bis(2-phenylbenzo[*b*]thiophene) (**2b**) in 97% isolated yield. The present reaction proceeded through two successive intramolecular carbon-sulfur bond addition reactions, or the so-called carbothiolation.

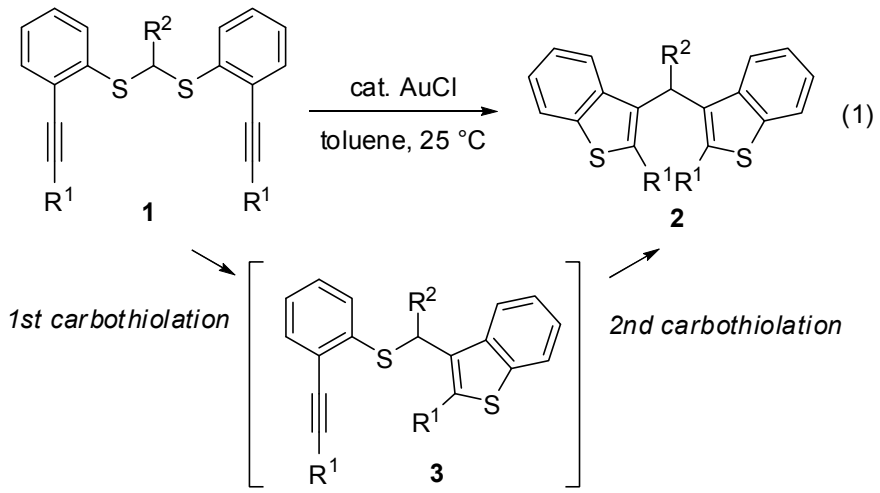
INTRODUCTION

Sulfur-containing polyarenes have recently received much attention as materials for organic molecular devices, such as organic semiconductors.[1,2] Because of this, the efficient synthesis of these molecules has gained prominence in organic synthesis. Recently, we have developed a highly efficient method to synthesize 2,3-disubstituted benzothiophenes, which involves the gold-catalyzed cyclization of *ortho*-alkynylphenyl alkyl sulfides (Scheme 1).[3,4] In this so-called carbothiolation reaction, various carbon functional groups, such as α-alkoxyalkyl, allyl, *p*-methoxyphenylmethyl (MPM), and α-phenethyl groups, are employed as the migrating group (E). This carbothiolation reaction proceeds via a

nucleophilic attack of the sulfur atom on the C-C triple bond that possesses enhanced electrophilicity due to its π coordination with the gold catalyst, and the subsequent 1,3-migration of the functional group (E) on the sulfur atom in the resulting cyclized intermediate **B**. Accordingly, we envisioned that bis(benzo[*b*]thiophen-3-yl)methanes (**2**), which are potential frameworks of sulfur-containing polyacenes, can be synthesized from bis(*ortho*-alkynylphenylthio)acetals (**1**) via two successive carbothiolation reactions (eq 1). In this case, we expected that both the 1-(arylthio)alkyl group of starting material (**1**) and the 1-(benzo[*b*]thiophen-3-yl)alkyl group in **3**, which is the product of the first carbothiolation, possess the migration ability from S to C. Herein, we report that the gold-catalyzed two successive cyclization reactions of thioacetals (**1**) produced bis(benzo[*b*]thiophen-3-yl)methanes (**2**) in good to excellent yields with high catalyst turnover numbers under mild reaction conditions.[5]

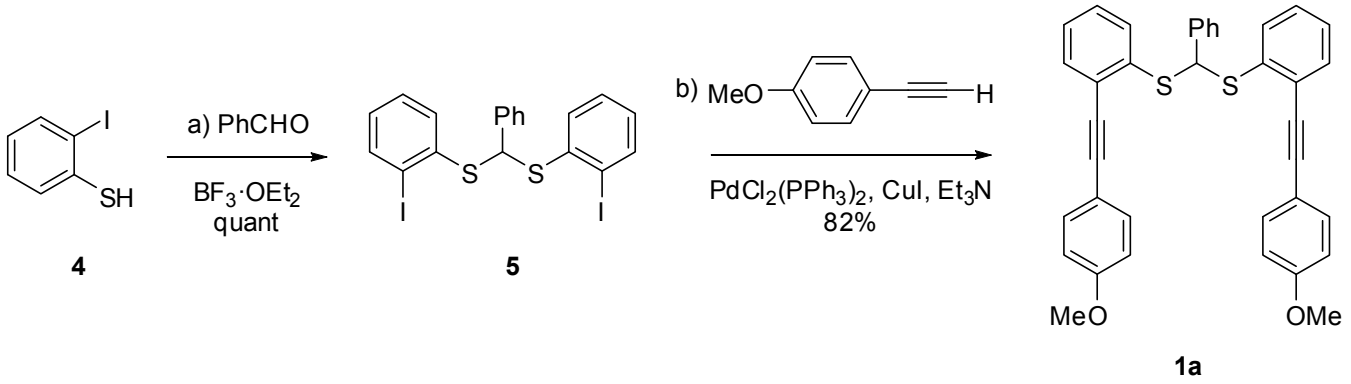


Scheme 1. Gold-catalyzed carbothiolation of *ortho*-alkynylphenyl sulfides



RESULTS AND DISCUSSION

Prior to the double carbothiolation, the substrates (**1**) were readily prepared from *o*-iodobenzenethiol (**4**) in two steps, as exemplified in Scheme 2 (preparation of **1a**). First, **4** was converted to the corresponding thioacetal **5** by condensation with an aldehyde in the presence of $BF_3 \cdot OEt_2$. The desired bis(*ortho*-alkynylphenylthio)acetals **1** were obtained by either Sonogashira coupling with an aryl or alkyl acetylene, or Negishi coupling with ethynylzinc bromide for preparation of **1h** (see Supporting Information).

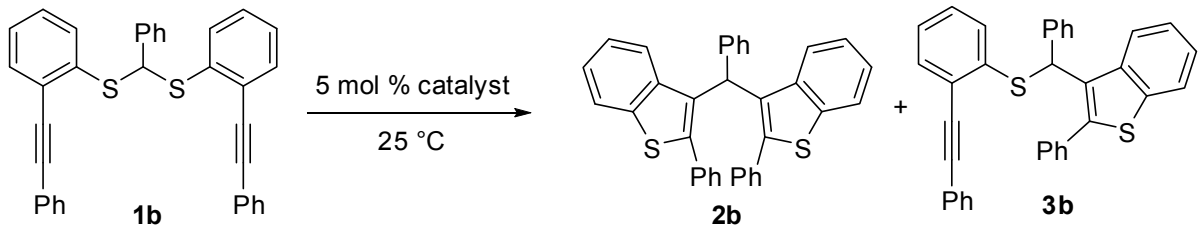


Scheme 2. Preparation of **1a**

a) $BF_3 \cdot OEt_2$, $CHCl_3$, 0 °C to rt. quant. b) $PdCl_2(PPh_3)_2$, CuI, Et_3N, rt. 82%.

The catalytic activity of various transition metal salts was tested using substrate **1b**, as summarized in Table 1, The reaction of **1b** in the presence of 5 mol % of AuCl in toluene at 25 °C for 1 hour gave **2b** quantitatively (entry 1). It should be noted that **2b** was afforded in excellent yield even with the use of 0.1 mol % of AuCl (entry 3). $AuCl_3$ and $AuBr_3$ also showed good catalytic activities (entries 4 and 5), while the reaction using Ag(OTf) as catalyst, instead of gold catalysts, gave **2b** in moderate yield (entry 6). In contrast to the gold catalysts, the reaction using platinum salts, such as $PtCl_2$, $PtCl_4$, and $PtBr_2$, afforded corresponding monocyclized product (**3b**) as the major product (entries 7-9).[6] $InBr_3$ and $PdCl_2$ did not promote the present reaction and starting material (**1b**) was recovered quantitatively (entries 10 and 11). Perhaps, highly carbophilic gold salts effectively catalyzed the present reaction before the the catalysts were poisoned by sulfur atoms of both the substrate and the product. The present reaction proceeded in various solvents, including toluene, CH_2Cl, ethyl acetate, and THF (entries 1, 12-14).

Table 1. Optimization of reaction conditions.

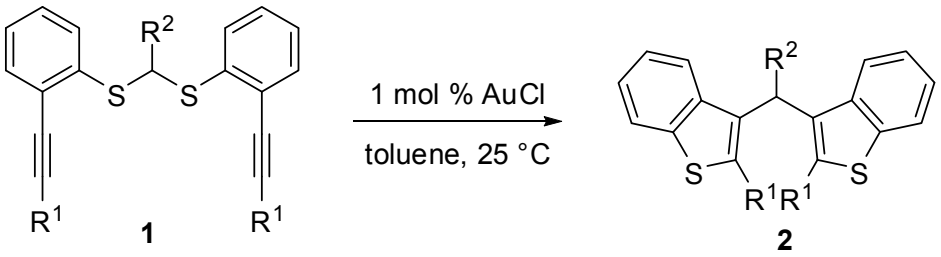


Entry	Catalyst	Solvent	Time / h	Yield of **2b** / % [a]	Yield of **3b** / % [a]
1	AuCl	toluene	1	Quant.	0
2	AuCl [b]	toluene	1	Quant. (97) [c]	0
3	AuCl [d]	toluene	24	Quant. (98) [c]	0
4	$AuCl_3$	toluene	1	Quant.	0
5	$AuBr_3$	toluene	1	Quant.	0
6	Ag(OTf)	toluene	24	52	0
7	$PtCl_2$	toluene	4.5	trace	91
8	$PtCl_4$	toluene	24	9	60
9	$PtBr_2$	toluene	24	0	79
10	$InBr_3$	toluene	24	0	0
11	$PdCl_2$	toluene	24	0	0
12	AuCl [e]	CH_2Cl_2	1	(97) [c]	0
13	AuCl [e]	EtOAc	1	(97) [c]	0
14	AuCl [e]	THF	1	(95) [c]	0

[a] The yield was determined by ^{1}H NMR using CH_2Br_2 as an internal standard.
[b] 1 mol % of AuCl was used.
[c] Isolated yield in parentheses.
[d] 0.1 mol % of AuCl was used.
[e] 0.5 mol % of AuCl was used.

Next, the optimal conditions (Table 1, entry 2) were employed for the cyclization reaction using various substrates (**1**), as summarized in Table 2. The reaction of **1a** and **1c** having an aromatic ring at the alkynyl terminus proceeded quickly irrespective of the electronic properties of the aromatic moiety (entries 1 and 2). Substrate (**1d**) bearing a normal alkyl group was converted into **2d** in good yield, while the reaction of **1e** having a bulky cyclohexyl group proceeded slowly, affording **2e** in moderate yield (entries 3 and 4). The reaction of **1g** having an alkyl group on the acetal carbon (R^2) gave desired product **2g** in good yield albeit requiring a prolonged reaction time (entry 6).

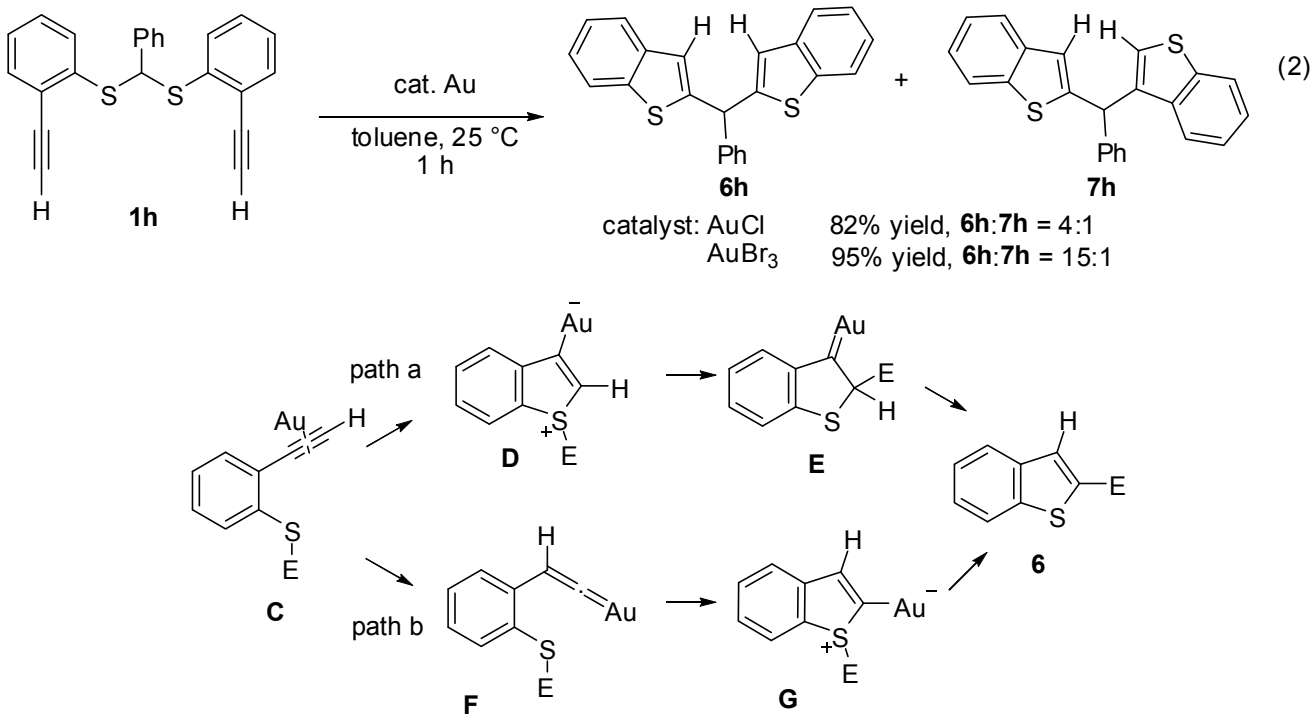
Table 2. AuCl-catalyzed double carbothiolation of **1**.[a]



entry	**1**	R^1	R^2	Time / h	**2**	Yield / % [b]
1	**1a**	*p*-$MeOC_6H_4$	Ph	1	**2a**	93
2	**1c**	*p*-$F_3CC_6H_4$	Ph	1	**2c**	98
3	**1d**	*n*-Pr	Ph	2.5	**2d**	89
4	**1e**	cyclohexyl	Ph	6	**2e**	55
5	**1f**	Ph	*p*-Cl-C_6H_4	1	**2f**	98
6	**1g**	Ph	*n*-Pr	30	**2g**	82

[a] The reaction of **1** (0.5 mmol) was carried out in the presence of 1 mol % of AuCl in toluene at 25 °C.
[b] Isolated yield.

In contrast to internal alkynes (**1a-g**), terminal alkyne (**1h**) was converted into bis(benzo[*b*]thiophen-2-yl)methane derivative (**6h**) as the main product, of which the two benzo[*b*]thiophene groups were tethered at the 2 position, along with a small amount of 2,3'-(methylene)dibenzo[*b*]thiophene derivative (**7h**) as byproduct (eq 2). When $AuBr_3$ was used as the catalyst, **6h** was obtained in excellent yield with good regioselectivity. It is presumed that the reaction of **1h** proceeds through the formation of gold-carbenoid intermediate **E** as a result of the 1,2-alkyl shift of vinylgold species **D** and the subsequent 1,2-hydrogen migration (Scheme 3, path a).[7,8] Alternatively, it is also possible that **4** was produced through the formation of vinylidene-gold intermediate **F**,[9] the nucleophilic attack of the sulfur atom on the α-carbon of the vinylidene moiety, and the carbodemetallation via the 1,2-alkyl shift (path b). Perhaps, the different result of the terminal alkyne (**1h**) from the internal alkynes (**1a-g**) is attributed to the high migration ability of a hydrogen atom at the alkyne terminus in either vinylidene formation (**C** to **F**) or 1,2- shift to the gold carbene (**E** to **6**).[10] Moreover, in the case of path a, less steric repulsion between the migrating group (E) and the least bulky hydrogen atom in the gold carbenoid intermediate **E** also facilitates the 1,2-alkyl shift from **D** to **E**.



Scheme 3

In conclusion, we have developed an efficient method to synthesize bis(benzo[*b*]thiophenyl)methanes in good to excellent yields. The application of the present methodology to the synthesis of sulfur-containing polyacenes is ongoing in our laboratory.

EXPERIMENTAL

Representative procedure. To a mixture of 1 mol % of AuCl and 0.4 mmol of **1** was added 2 mL of toluene in a pressure vial (Wheaton v-vial) at room temperature and the mixture was stirred at 25 °C. After confirming complete consumption of the starting material by TLC, the reaction mixture was passed through a short pad of silica gel with ethyl acetate. After the solvents were removed in vacuo, the residue was purified by silica gel column chromatography using hexane/CH_2Cl_2 (10:1) as eluent to give product **2**.

3,3'-(Phenylmethylene)bis(2-(4-methoxyphenyl)benzo[*b*]thiophene) (2a). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (s, 6H), 6.26 (s, 1H), 6.53-6.56 (m, 4H), 6.91-6.94 (m, 4H), 6.95-7.01 (m, 4H), 7.11-7.12 (m, 2H), 7.15-7.20 (m, 5H), 7.70 (d, *J* = 7.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.70, 55.15, 113.20, 121.58, 123.35, 123.72, 124.13, 126.25, 126.44, 128.36, 129.20, 130.55, 131.86, 138.75, 140.05, 141.26, 142.21, 159.02. IR (neat) 3060, 2955, 2835, 1608, 1497, 1433, 1291, 1248, 1175, 1033, 829 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 591.1423, found. 591.1422.

3,3'-(Phenylmethylene)bis(2-phenylbenzo[*b*]thiophene) (2b). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.28 (s, 1H), 6.96-7.04 (m, 13H), 7.06-7.10 (m, 2H), 7.16-7.19 (m, 6H), 7.70 (d, *J* = 7.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.82, 121.68, 123.56, 123.82, 124.18, 126.52, 127.64, 128.37, 129.27, 129.43, 132.01, 133.97, 138.90, 140.01, 141.38, 142.10. IR (neat) 3728, 3705, 3628, 3590, 3048, 3022, 1600, 1434, 1077, 1027 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 531.1212, found. 531.1211.

3,3'-(Phenylmethylene)bis(2-(4-(trifluoromethyl)phenyl)benzo[*b*]thiophene) (2c). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.24 (s, 1H), 7.01-7.03 (m, 4H), 7.07 (d, *J* = 8.1 Hz, 4H), 7.12-7.14 (m, 2H), 7.21-7.25 (m, 5H), 7.27 (d, *J* = 8.1 Hz, 4H), 7.72 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.79, 121.93, 123.86 (q, ^{1}J (C, F) = 272.8 Hz), 124.19, 124.25, 124.29, 234.65 (q, ^{3}J (C, F) = 3.8 Hz), 127.01, 128.67, 129.16, 129.59, 129.73 (q, ^{2}J (C, F) = 32.7 Hz), 132.78, 137.57, 138.94, 139.53, 139.58, 141.18. IR (neat) 3060, 1615, 1320, 1164, 1127, 1066, 1018 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 667.0959, found. 667.0956.

3,3'-(Phenylmethylene)bis(2-propylbenzo[*b*]thiophene) (2d). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.63 (t, *J* = 7.3 Hz, 6H), 1.29-1.46 (m, 4H), 2.36-2.48 (m, 4H), 6.34 (s, 1H), 7.08-7.11 (m, 2H), 7.16-7.12 (m, 6H), 7.25-7.28 (m, 3H), 7.75 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.84, 24.46, 31.10, 44.30, 121.99, 122.24, 123.28, 123.83, 126.74, 128.51, 129.08, 130.17, 137.95, 140.54, 141.27, 143.76. IR (neat) 3060, 2958, 2929, 2870, 1601, 1493, 1456, 1435, 1151, 1027 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 463.1525, found. 463.1522.

3,3'-(Phenylmethylene)bis(2-cyclohexylbenzo[*b*]thiophene) (2e). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.59 (dtt, *J* = 12.8, 12.8, 3.4 Hz, 2H), 0.68 (dtt, *J* = 12.8, 12.8, 3.4 Hz, 2H), 1.05 (ddddd, *J* = 12.8, 12.8, 12.8, 3.4, 3.4 Hz, 2H), 1.16-1.24 (m, 2H), 1.26-1.34 (m, 4H), 1.45-1.59 (m, 8H), 2.60 (tt, *J* = 11.8, 3.4 Hz, 2H), 6.42 (s, 1H), 7.08-7.13 (m, 4H), 7.18 (ddd, *J* = 8.1, 6.4, 1.7 Hz, 1H), 7.20 (ddd, *J* = 8.1, 6.4, 1.7 Hz, 1H), 7.24-7.31 (m, 5H), 7.76 (d, *J* = 7.7 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.71, 26.24, 26.39, 35.19, 35.48, 38.30, 44.34, 122.22, 122.45, 123.15, 123.66, 126.79, 128.58, 129.05, 129.36, 137.82, 140.10, 141.21, 150.31. IR (neat) 3061, 2925, 2850, 1494, 1448, 1153, 1025 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 543.2151, found. 543.2150.

3,3'-((4-Chlorophenyl)methylene)bis(2-phenylbenzo[*b*]thiophene) (2f). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23 (s, 1H), 6.97-6.99 (m, 4H), 7.01-7.07 (m, 10H), 7.08-7.12 (m, 4H), 7.20 (ddd, *J* = 8.0, 6.3, 1.3 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.35, 121.77, 123.73, 123.90, 123.98, 127.72, 128.46, 129.42, 130.59, 131.35, 132.24, 133.79, 138.90, 139.74, 140.57, 141.62. IR (neat) 3060,

3025, 1600, 1488, 1432, 1092, 1014, 823 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 565.0822, found. 565.0821.

3,3'-(Butane-1,1-diyl)bis(2-phenylbenzo[*b*]thiophene) (2g). ^1H NMR (500 MHz, $CDCl_3$) δ 0.58 (t, *J* = 7.3 Hz, 3H), 1.05-1.15 (m, 2H), 2.09-2.14 (m, 2H), 4.96 (t, *J* = 7.8 Hz, 1H), 7.07-7.18 (m, 12H), 7.22-7.23 (m, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.61, 21.39, 36.14, 39.91, 121.71, 123.40, 123.59, 123.87, 127.64, 127.73, 129.88, 133.28, 134.76, 138.88, 139.79, 140.27. IR (neat) 3060, 2958, 2871, 1601, 1456, 1434, 1212, 1075, 1028 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 497.1368, found. 497.1368.

2,2'-(Phenylmethylene)dibenzo[*b*]thiophene (6h). ^1H NMR (500 MHz, $CDCl_3$) δ 5.94 (s, 1H), 7.08 (s, 2H), 7.21-7.31 (m, 5H), 7.33-7.36 (m, 2H), 7.38-7.40 (m, 2H), 7.64 (d, *J* = 6.8 Hz, 2H), 7.73 (dd, *J* = 7.9, 0.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 48.81, 122.20, 123.11, 123.44, 124.13, 124.26, 127.54, 128.57, 128.66, 139.47, 139.93. 142.10, 147.30. IR (neat) 3058, 3027, 1600, 1493, 1456, 1434, 1154, 1071, 859 cm^{-1}. HRMS (ESI) calcd. for $(M+Na)^+$ 379.0586, found. 379.0586.

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