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Regioselective palladium-catalyzed cross-coupling reactions in the synthesis of novel 2,3-disubstituted thiophene derivatives

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Abstract—A reactivity optimization study of the palladium-catalyzed cross-coupling reactions of 2,3-dibromothiophene and organometallic reagents has been conducted. Regioselective coupling at the C2 position, accomplished most notably by Suzuki coupling, was combined with a Stille reaction at C3 using Fu's modification, to afford the 2,3-disubstituted thiophene derivatives.

1. Introduction

The preparation of polyfunctionalized heterocyclic compounds is of interest in research fields as diverse as natural product synthesis, drug design, molecular recognition and materials science. In this regard, thiophene-based compounds are considered an important class of materials which show intrinsic electronic properties such as luminescence, redox activity and electron-transport. Over the past few years, the isolation of naturally occurring thiophene derivatives has stimulated much interest as a consequence of their wide range of photobiological activities.[1,2] This has led in turn to the biologically-guided synthesis of novel thiophene-containing compounds.[3–6]

Given the ready availability of halogenated thiophenes and the current development of metal-catalyzed cross-coupling chemistry, it is not unexpected that most of these synthetic thiophene derivatives have been prepared by applying transition metal-catalyzed carbon–carbon bond-forming reactions. Representative examples of the use of the Tamao–Kumada–Corriu,[3,7] Negishi,[7c,8] Sonogashira,[3,7e,9] Suzuki,[4,5,10] Stille[3,4,11] and Heck[12] couplings have been reported in the literature. By contrast, there are only a few reports on the use of dihalogenated thiophenes as electrophilic components in metal-catalyzed cross-coupling reactions.[7c,8c,d,10a,b,13,14]

In connection with a project directed at the preparation of novel 2,3-disubstituted thiophene derivatives, we reasoned that 2,3-dibromothiophene **1**, easily prepared from 3-bromothiophene,[15] could become a valuable starting material. Regioselective palladium-catalyzed cross-coupling processes would allow differentiation between the two reactive positions (C2 and C3) and, consequently, selective introduction of two differently functionalized alkenyl, aryl or alkynyl chains.

The recent report describing regioselective coupling reactions of 2,3-dibromofuran[16] prompted us to disclose our findings on the reactivity of 2,3-dibromothiophene **1** using a variety of palladium-catalyzed cross-coupling reactions with organometallic reagents.

2. Results and discussion

2.1. Regioselective Pd (0)-catalyzed coupling at carbon atom C2

The Sonogashira coupling,[17] i.e. the reaction of organic electrophiles with copper acetylides, generated in situ from the corresponding terminal alkynes, has become the method of choice for the preparation of internal alkynes, aryl alkynes or enynes. The active Pd (0) species required for the catalytic cycle is produced from the Pd (II) pre-catalyst following an initial alkyne dimerization process. The choice of reaction conditions (solvent, temperature…) depends on the reactivity of the starting halide, although a tertiary amine is required for neutralizing the HX formed along the cycle.

2,3-Dibromothiophene **1** was reacted with a series of alkynes under the conditions previously reported [$Pd(PPh_3)_2Cl_2$, Et_3N, CuI, Ph_3P, 60°C],[13] and the results are listed in Table 1. TMS-acetylene **2a** (entry 1) was included in the survey in order to corroborate the results reported by Brandsma et al.[13] Alkynes **2f**,[18] **2g**[19] and **2h**[†]

Keywords: thiophenes; Sonogashira reactions; Stille reactions; Suzuki reactions; heterocycles.

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[†] Alkyne **2h** is commercially available.

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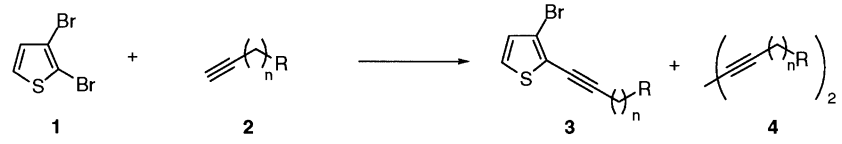
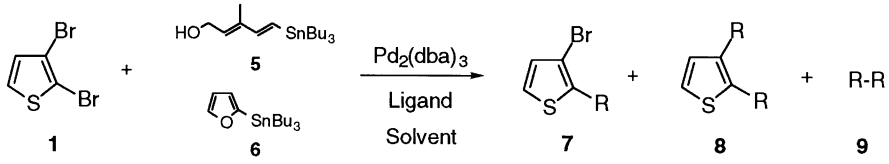
Table 1. Sonogashira coupling reactions of 2,3-dibromothiophene **1** with terminal alkynes

Entry	Alkyne	Reaction conditions[a]	T (°C)	t (h)	Yield (%)		**1/3** Ratio[b]
					3	**4**	
1	**2a** (n=0, R=TMS)	A	60	3	56	ND[c]	–
2	**2b** (n=1, R=OH)	A	60	3	12	32[d]	1/1
3	**2c** (n=2, R=OH)	A	60	2	11	42[d]	2.3/1
4	**2d** (n=3, R=OH)	A	60	3	60	32[d]	1/2
5	**2e** (n=4, R=OH)	A	60	2.5	56	25[d]	1/4
6	**2f** (n=5, R=OH)	A	80	3	20	56	3/1
7	**2g** (n=6, R=OH)	A	60	3	20	55	2.3/1
8	**2h** (n=7, R=OH)	A	60	3	42	43	1/2
9	**2i** (n=4, R=OTBDMS)	A	60	3	42	40	1/1
10	**2j** (n=3, R=CH_3)	A[e]	84	2	–[f]	–[f]	4/1

[a] Conditions: A: **1** (1 mol equiv.), **2** (1.1 mol equiv.), $Pd(PPh_3)_2Cl_2$ (0.004 mol equiv.), CuI (0.008 mol equiv.), Ph_3P (0.005 mol equiv.), Et_3N.
[b] Starting material/product ratio determined by integration of the ^1H NMR spectra.
[c] ND: Not determined due to its volatility.
[d] Dimeric products **4b**, **4c**, **4d** and **4e** are commercially available.
[e] iPr_2NH used instead of Et_3N.
[f] An inseparable mixture of 2,3-dibromothiophene **1**, product **3j** and alkyne dimer **4j** was obtained. Integration of its ^1H NMR spectrum showed a **1/3j/4j** ratio of 4:1:2.



Scheme 1.



Scheme 2.

were prepared by isomerization of the corresponding internal alkynes.[18] Protection of commercially available hex-5-yn-1-ol as *tert*-butyldimethylsilyl ether provided known compound **2i**.[20] Since the quality of the copper catalyst is a crucial factor for the success of these type of organometallic processes, we rigorously purified this salt following literature procedures.[21] Addition of PPh_3 is required to avoid deposition of Pd (0) due to the high temperatures needed to induce coupling of aryl and heteroaryl bromides, which are particularly unreactive if no electron-withdrawing substituents are present on the ring.

The reactions of 2,3-dibromothiophene **1** and alkynes **2** are regioselective processes which yield, in agreement with Brandsma's finding with TMS-acetylene **2a** (entry 1),[13] the C2 modified compound **3** as the only substitution product. However, the corresponding diynes **4** were also isolated in variable amounts.‡ Whereas the reaction of **1** with pent-4-yn-1-ol **2d** or hex-5-yn-1-ol **2e** (entries 4 and 5) proceeds in a moderate yield (60 and 56%, respectively) to give the monosubstituted products **3d** and **3e**, together with the alkyne dimerization product (32 and 25%, respectively), in the case of alkynes **2b**, **2c**, **2f**, **2g** and **2j** (entries 2, 3, 6, 7 and 10) the coupling is very slow, proceeding with low conversion rates, and leading to the isolation of the alkyne dimer as the main product. Since alkyne dimers (in amounts greater than those generated on forming the 14-electron PdL_2 complex)[17] are the most common by-products in the Sonogashira coupling reactions, there has been much synthetic effort devoted to finding new experimental procedures to avoid this undesired pathway.[22] Several of these modifications (changes in the base, catalyst, solvent, amount of alkyne, use of cosolvents) have been tried in our case with alkyne **2j** without success. Alkynes **2h** and **2i** (entries 8 and 9) proved to be slightly more reactive, although the mono-substituted product **3** was isolated in a disappointing 42% yield, and dimerization was an important competing process for alkyne consumption (Scheme 1).

Given the low reactivity of 2,3-dibromothiophene, the recent report by Buchwald and Fu[23] describing the room temperature Sonogashira coupling of aryl bromides, using the accelerating effect of a bulky trialkylphosphine, was taken into consideration. In our hands, however, the modification $[Pd(PhCN)_2Cl_2/PtBu_3]$ proved ineffective with alkynes **2e** and **2j**, leading to very slow reactions at room temperature (less than 50% conversion after 48 h). The

‡ It must be mentioned that alkyne dimer **4a** was also detected, although it could not be isolated due to its high volatility.

Table 2. Stille cross-coupling of 2,3-dibromothiophene **1** with organostannanes **5** and **6**

Entry	Stannane	Mol equiv. [RsnBu$_3$]	Reaction conditions[a]	T (°C)	t (h)	Yield (%)		
						7	**8**	**9**
1	**5**	1.1	A	45	1.5	59	12	ND[b]
2	**5**	1.5	A	45	1.5	70	9	ND[b]
3	**6**	1.1	A	40	6	17	ND[b]	–
4	**6**	1.1	A	60	1.5	45	ND[b]	–
5	**6**	1.5	A	60	1	70	4	–
6	**5**	1.1	B	25	2	71	16	–
7	**5**	1.5	B	25	1	67	31	–
8	**5**	1.5	B	25	2	65	25	–
9	**5**	2.1	B	25	7	25	71	–
10	**6**	1.1	B	25	2	72	11	–
11	**6**	1.5	B	25	1	41	33	–
12	**6**	1.5	B	25	5.5	34	31	–

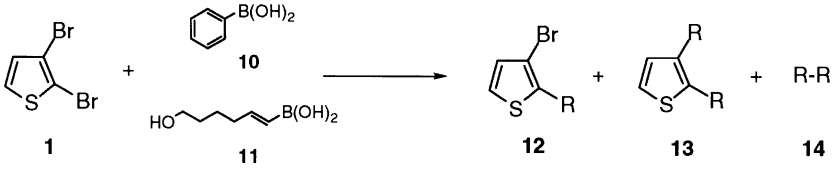
[a] Conditions: A: **1** (1 mol equiv.), $Pd_2(dba)_3$ (0.02 mol equiv.), $AsPh_3$ (0.2 mol equiv.), NMP. B: **1** (1 mol equiv.), $Pd_2(dba)_3$ (0.01 mol equiv.), PtBu$_3$ (0.05 mol equiv.), CsF (2 mol equiv.), dioxane.
[b] ND: Not determined.

alkyne dimer was again the main product on heating the mixture to 60°C.

The coupling of 2,3-dibromothiophene **1** with different organostannanes under the Stille reaction conditions[24] was also explored (Scheme 2). We first selected the modified reaction conditions developed by Farina[25] [$Pd_2(dba)_3$/$AsPh_3$ as palladium/ligand combination in NMP]. Table 2 shows the results obtained for the coupling of dibromide **1** and representative alkenyl (**5**)[26] and heteroaryl (**6**)[27] organotin compounds. The coupling took place regioselectively at C2, although the disubstituted product **8** was also obtained in low yields (entries 2 and 5). It must be pointed out as well that minor amounts of the organostannane dimer **9** (entries 1 and 2) were detected in the coupling of dienyl stannane **5** under Farina's conditions.

We also explored Fu's modification of the Stille reaction that uses PtBu$_3$ as palladium ligand and CsF to activate the tin reagent.[28] As expected, this modification led to an increase in the reactivity of 2,3-dibromothiophene, with the coupling to stannanes proceeding at room temperature in short reaction times (entries 6, 7, 8, 10 and 11). Unfortunately, the greater reactivity translated into a reduced discrimination of both C–Br bonds by the stannane, and a significant decrease in the regioselectivity was observed (entries 7, 8, 11 and 12).

The reactions of 2,3-dibromothiophene under the Suzuki coupling conditions[29] (Scheme 3) are summarized in Table 3. The scope and limitations of this coupling were analyzed using an aryl (**10**) and a vinyl boronic acid (**11**).[30] The classical Suzuki reaction conditions [$Pd(PPh_3)_4$ and

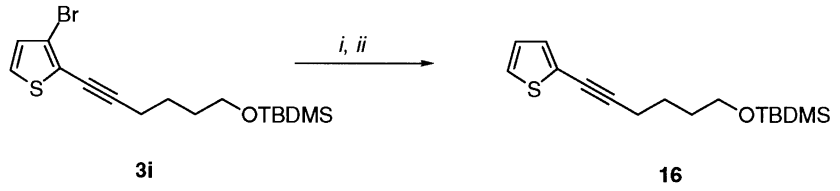


Scheme 3.

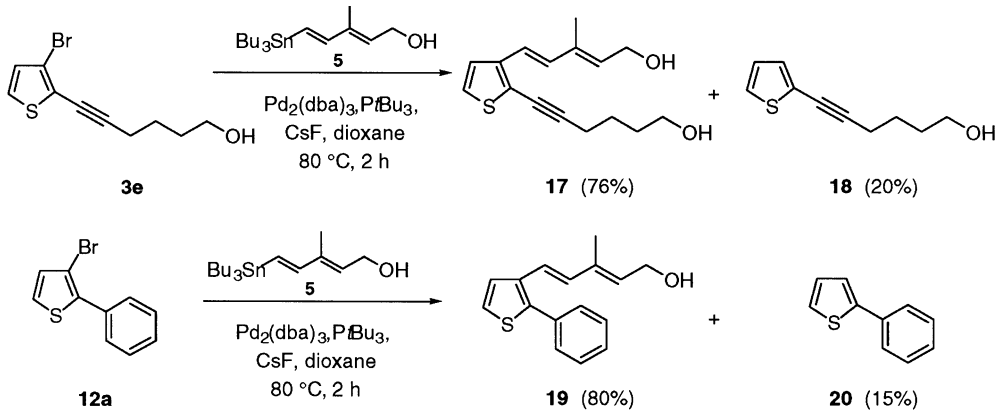
Table 3. Suzuki cross-coupling of 2,3-dibromothiophene **1** with boronic acids **10** and **11**

Entry	Organoborane	Mol equiv. [R–B(OH)$_2$]	Reaction conditions[a]	T (°C)	t (h)	Yield (%)		
						12	**13**	**14**
1	**10**	1.1	A	100	4	81	2	–
2	**11**	2.5	A	55	4.5	65	–	62
3	**11**	2.5	B	25	6	51	–	21
4	**10**	1.5	C	100	4	40	8	–
5	**10**	1.5	C	100	8	40	8	–
6	**11**	1.5	D[b]	55	4.5	46	7	ND[c]
7	**11**	2.5	D[b]	55	4.5	44	7	–
8	**11**	2.5	D[d]	90	5	64	12	–

[a] Conditions: A: **1** (1 mol equiv.), $Pd(PPh_3)_4$ (0.08 mol equiv.), K_2CO_3 (4 mol equiv.), dioxane. B: **1** (1 mol equiv.), $Pd(PPh_3)_4$ (0.1 mol equiv.), 10% TlOH (5 mol equiv.), THF. C: **1** (1 mol equiv.), $Pd(OAc)_2$ (0.01 mol equiv.), K_3PO_4 (2 mol equiv.), **15** (0.02 mol equiv.), toluene. D: **1** (1 mol equiv.), $Pd(OAc)_2$ (0.01 mol equiv.), KF (3 mol equiv.), **15** (0.02 mol equiv.).
[b] THF was used as solvent.
[c] ND: Not determined.
[d] Dioxane was used as solvent.



Scheme 4. (i) *sec*-BuLi, THF; (ii) MeOH.



Scheme 5.

K_2CO_3 in refluxing dioxane] were adopted first, the results of which are shown in Table 3 (entries 1 and 2).

Phenylboronic acid **10** reacted smoothly with 2,3-dibromothiophene under these conditions to yield the monosubstituted product **12a**[31] (81%) together with a small amount (2%) of the bis-substituted product **13a**[§] (entry 1). Vinylboronic acid **11** led exclusively to the C2-substituted product **12b**, although in this case boronic acid dimerization seems to be an important competing process (entry 2). Application of Kishi's modification[32] (TlOH, THF, room temperature) to the reaction of **11** and **1** gave similar results, namely regioselective substitution at position 2 (51% yield of **12b**), together with the competing process of boronic acid dimerization (entry 3). We also explored the improved procedure recently reported by Buchwald[33] for the room temperature Suzuki coupling of aryl bromides, or the even less-reactive aryl chlorides, with aryl boronic acids. This modification, the use of palladium acetate and *o*-(di-*tert*-butylphosphino)biphenyl (**15**) in different base/solvent systems, proved inefficient, requiring instead more drastic conditions (toluene, 100°C, 8 h; entry 5), with low yields (entries 4, 5, 6 and 7) and poor regioselectivity (entry 8).

The regioselective introduction of the substituent at the C2 position of 2,3-dibromothiophene through Sonogashira, Stille and Suzuki couplings was confirmed by the analysis of the debromination product, generated upon treatment of compound **3i** with *sec*-BuLi followed by a MeOH quench. ^{1}H NMR analysis of thiophene chemical shifts and coupling constants pattern for product **16** unequivocally showed that the new hydrogen atom had been incorporated at position 3 (Scheme 4).

[§] 2,3-Diphenylthiophene is commercially available.

Considering that the three variants of the palladium-catalyzed cross-coupling reactions share the first oxidative addition step, it is concluded that the oxidative addition of Pd (0) at position 2 of 2,3-dibromothiophene **1** is favored over that at C3, which eventually determines the regioselectivity of the reaction. The facile oxidative addition into the carbon–bromine bond at position 2 must be a consequence of the inherent higher electrophilicity of C2 over C3, as well as the lower double bond character of C3–C4 vs C2–C3, as it seems to be the case for 2,3-dibromofuran.[16]

2.2. Pd (0)-catalyzed cross-coupling at carbon atom C3

In order to prove the synthetic potential of 2,3-dibromothiophene, further substitution at C3 position of the thiophene nucleus was required. Prompted by the previous finding that the modified Stille reaction conditions developed by Fu[28] provided an enormous increase in the reactivity of position C3, we treated 3-bromo-2-substituted thiophenes **3e** and **12a**, in dioxane containing CsF, with dienyl stannane **5** in the presence of catalytic quantities of $Pd_2(dba)_3$ and P*t*Bu$_3$ (Scheme 5). Disubstituted products **17** and **19** were obtained in good yields (76 and 80%, respectively), along with the hydrodebromination product at C3 position. This side reaction perhaps suggests an ineffective transmetalation or reductive elimination in the overall cycle.

3. Summary and conclusion

2,3-Dibromothiophene **1** undergoes regioselective Pd (0)-catalyzed cross-coupling reactions at C2 with a variety of organometallic reagents. The observed regioselectivity is most likely due to the electron deficiency at this position, which renders a facile oxidative addition of Pd (0) in the C–Br bond. According to the experimental findings, the Suzuki coupling led to the highest regioselectivity. Stille

conditions are less convenient, since the disubstituted thiophene is obtained in greater proportion than using the Suzuki reaction. Sonogashira coupling, in contrast, gave inconsistent results, depending upon the alkyne structure. Pd (0)-catalyzed coupling at the less-reactive C3–Br is by far more challenging. It was nevertheless accomplished through Fu's modification of the Stille reaction. Ready access to 2,3-disubstituted thiophenes is therefore possible by means of a two-step strategy that makes use of consecutive Pd (0)-catalyzed cross-coupling reactions with organometallic compounds.

4. Experimental

4.1. General

Solvents were dried according to published methods and were distilled before use. HPLC grade solvents were used for HPLC purifications. All other reagents were commercial compounds of the highest purity available. Analytical thin-layer chromatography (TLC) was performed using Merck silica gel (60 F-254) plates (0.25 mm) precoated with a fluorescent indicator. Column chromatography was performed using Merck silica gel 60 (particle size 0.040–0.063 μm). Bulb-to-bulb distillations were carried out on a Kugelrohr apparatus; boiling points refer to air bath temperatures and are uncorrected. Melting points (mp) were measured on a Gallenkamp apparatus and are uncorrected. Proton (^{1}H) and carbon (^{13}C) magnetic resonance spectra (NMR) were recorded on a Bruker AMX-400 [400 MHz (100 MHz for ^{13}C)] Fourier transform spectrometer, and chemical shifts are expressed in parts per million (δ) relative to tetramethylsilane (TMS, 0 ppm), dichloromethane (CH_2Cl_2, 5.32 ppm for ^{1}H and 53.8 ppm for ^{13}C), acetone (CH_3COCH_3, 2.05 ppm for ^{1}H and 29.8 and 206.5 ppm for ^{13}C) or chloroform ($CHCl_3$, 7.24 ppm for ^{1}H and 77.00 ppm for ^{13}C) as internal reference. ^{13}C multiplicities (s, singlet; d, doublet; t, triplet; q, quartet) were assigned with the aid of the DEPT pulse sequence. Infrared spectra (IR) were obtained on a MIDAC Prospect Model FT-IR spectrophotometer. Absorptions are recorded in wavenumbers (cm^{-1}). Low-resolution mass spectra were taken on an HP59970 instrument operating at 70 eV. High-resolution mass spectra were taken on a VG Autospec M instrument.

4.1.1. Oct-7-yn-1-ol (2g). *General procedure for alkynol isomerization*. Lithium wire (0.17 g, 24.50 mmol), thoroughly washed first with hexane and then with 95:5 hexane/EtOH mixture, was suspended on 1,2-diaminoethane (9.60 mL) and heated to 70°C for 1 h. After cooling down to 25°C, potassium *tert*-butoxide (1.80 g, 15.80 mmol) was added in one portion and the mixture was stirred at 25°C for 1 h. Oct-3-yn-1-ol (0.50 g, 3.96 mmol) was then added dropwise, and the final reaction mixture was stirred at 25°C for 3 h, after which time it was poured into ice. The mixture was then extracted with CH_2Cl_2 (3×10 mL) and the combined organic extracts were washed with 10% HCl (3×30 mL). The resulting aqueous layer was extracted with CH_2Cl_2 (2×90 mL) and the combined organic phases were finally dried (Na_2SO_4) and evaporated. Distillation of the residue (85°C/0.5 mm Hg; lit.[19] 90–94°C/4 mmHg) gave 0.48 g (96%) of oct-7-yn-1-ol (**2g**) as a colorless oil.

4.1.2. Non-8-yn-1-ol (2h). According to the general procedure for alkynol isomerization, the reaction of non-2-yn-1-ol (0.30 g, 2.14 mmol) afforded, after distillation (100°C/0.5 mmHg), 0.26 g (85%) of alkynol **2h** as a colorless oil.

4.1.3. *tert*-Butyldimethylsilyl hex-5-yn-1-yl ether (2i). To a solution of hex-5-yn-1-ol (0.30 g, 3.06 mmol) in DMF (7 mL) was added imidazol (0.50 g, 7.65 mmol), followed by *tert*-butyldimethylsilyl chloride (0.60 g, 4.28 mmol). After stirring at 25°C for 1 h, the mixture was diluted with H_2O and extracted with *tert*-butyl methyl ether (TBME) (3×10 mL). The combined organic layers were washed with H_2O (7×30 mL), dried (Na_2SO_4) and evaporated. Purification of the residue by chromatography (SiO_2, 95:5 hexane/AcOEt) afforded 0.60 g (92%) of a colorless oil identified as alkyne **2i**.

4.1.4. 3-Bromo-2-(2-trimethylsilylethyn-1-yl)thiophene (3a). *General procedure for the Sonogashira reaction*. To a stirred solution of 2,3-dibromothiophene **1** (0.20 g, 0.83 mmol) in Et_3N (1 mL) was added dropwise, a solution of trimethylsilylacetylene **2a** (0.08 g, 0.83 mmol) in Et_3N (1 mL), followed by $Pd(PPh_3)_2Cl_2$ (2.3 mg, 0.003 mmol) and PPh_3 (1.1 mg, 0.004 mmol), and the mixture was heated to 35°C for 10 min. CuI (1.2 mg, 0.006 mmol) was then added, and the reaction mixture was stirred at 60°C for 3 h. After cooling down to 25°C, the mixture was diluted with AcOEt, poured into H_2O and extracted with AcOEt (3×5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Purification by chromatography (SiO_2, hexane) afforded 0.12 g (56%) of 3-bromo-2-(2-trimethylsilylethyn-1-yl)thiophene (**3a**) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.25 (s, 9H, $Si(CH_3)_3$), 6.91 (d, J=5.4 Hz, 1H, H4), 7.14 (d, J=5.4 Hz, 1H, H5); ^{13}C NMR (100 MHz, $CDCl_3$) δ −0.2 (q, 3×, $Si(CH_3)_3$), 95.5 (s), 103.4 (s), 116.6 (s), 120.8 (s), 127.0 (d), 129.9 (d); IR (KBr, film) ν 3108 (w, =C–H), 2961 (m, C–H), 2899 (w, C–H), 2149 (s, C≡C), 1500 (m), 1419 (m), 1347 (m), 1250 (s), 1175 (m), 1146 (m), 1080 (m), 865 (s), 760 (s), 711 (s), 649 (m), 609 (m); MS *m/z* (%) 260 (M^+ [^{81}Br], 30), 258 (M^+ [^{79}Br], 28), 246 (14), 245 (100), 244 (13), 243 (94); HRMS calcd for $C_9H_{11}{}^{81}BrSSi$ 259.9514 and $C_9H_{11}{}^{79}BrSSi$ 257.9534, found 259.9514 and 257.9536.

4.1.5. 3-(3-Bromothien-2-yl)prop-2-yn-1-ol (3b). In accordance to the general procedure described above, the reaction of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with prop-2-yn-1-ol **2b** (0.03 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol), and CuI (0.6 mg, 0.003 mmol), for 3 h at 60°C, provided, after purification by chromatography (SiO_2, 99:1–95:5 CH_2Cl_2/MeOH), 11 mg (12%) of a colorless solid (mp 56.6°C, CH_2Cl_2/hexane) identified as 3-(3-bromothien-2-yl)prop-2-yn-1-ol (**3b**), and 8 mg (32%) of a colorless solid (mp 110.8°C, CH_2Cl_2) identified as hexa-2,4-diyn-1,6-diol (**4b**). *Data for* **3b**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 1.88 (d, J=6.2 Hz, 1H, OH), 4.51 (d, J=6.3 Hz, 2H, 2H1), 6.98 (d, J=5.4 Hz, 1H, H4′), 7.26 (d, J=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 51.5

(t, C1), 76.7 (s), 95.4 (s), 116.1 (s), 120.0 (s), 127.5 (d), 130.0 (d); IR (KBr, film) ν 3600–3100 (br, O–H), 3108 (m, =C–H), 2921 (m, C–H), 2859 (m, C–H), 2223 (m, C≡C), 1506 (m), 1429 (s), 1349 (s), 1206 (m), 1152 (m), 1021 (s), 864 (s), 712 (s), 607 (m); MS *m/z* (%) 219 ($[M+1]^+$ [^{81}Br], 8), 218 (M^+ [^{81}Br], 89), 217 ($[M+1]^+$ [^{79}Br], 33), 216 (M^+ [^{79}Br], 89), 215 (20), 137 (100), 109 (46), 108 (23), 65 (22), 63 (20); HRMS calcd for $C_7H_5{}^{81}BrOS$ 217.9224 and $C_7H_5{}^{79}BrOS$ 215.9244, found 217.9217 and 215.9239.

4.1.6. 4-(3-Bromothien-2-yl)but-3-yn-1-ol (3c). Following the general procedure for the Sonogashira reaction, treatment of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with but-3-yn-1-ol **2c** (0.03 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 2 h at 60°C, afforded 11 mg (11%) of compound **3c** as a yellow oil and 13 mg (42%) of a colorless solid (mp 49.3°C, CH_2Cl_2) identified as octa-3,5-diyn-1,8-diol (**4c**). *Data for* **3c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 (br s, 1H, OH), 2.73 (t, *J*=6.2 Hz, 2H, 2H2), 3.82 (t, *J*=6.2 Hz, 2H, 2H1), 6.91 (d, *J*=5.4 Hz, 1H, H4′), 7.12 (d, *J*=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.2 (t, C2), 60.8 (t, C1), 74.2 (s), 94.9 (s), 115.7 (s), 120.9 (s), 126.3 (d), 129.8 (d); IR (KBr, film) ν 3600–3100 (br, O–H), 3107 (m, =C–H), 2942 (m, C–H), 2886 (m, C–H), 2229 (w, C≡C), 1506 (m), 1428 (m), 1348 (m), 1044 (s), 864 (s), 710 (s), 607 (m); MS *m/z* (%) 233 ($[M+1]^+$ [^{81}Br], 8), 232 (M^+ [^{81}Br], 79), 230 (M^+ [^{79}Br], 78), 202 (36), 201 (100), 200 (36), 199 (98), 121 (46), 120 (26); HRMS calcd for $C_8H_7{}^{81}BrOS$ 231.9380 and $C_8H_7{}^{79}BrOS$ 229.9401, found 231.9385 and 229.9406.

4.1.7. 5-(3-Bromothien-2-yl)pent-4-yn-1-ol (3d). According to the general procedure described above, the reaction of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with pent-4-yn-1-ol **2d** (0.03 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 3 h at 60°C, afforded 0.06 g (60%) of alkynol **3d** as a yellow oil and 12 mg (32%) of a colorless solid (mp 45°C, CH_2Cl_2) identified as deca-4,6-diyn-1,10-diol (**4d**). *Data for* **3d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.67 (br s, 1H, OH), 1.86 (app. quintuplet, *J*=6.5 Hz, 2H, 2H2), 2.58 (t, *J*=6.9 Hz, 2H, 2H3), 3.82 (t, *J*=6.1 Hz, 2H, 2H1), 6.90 (d, *J*=5.4 Hz, 1H, H4′), 7.09 (d, *J*=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.3 (t, C2), 31.0 (t, C3), 61.5 (t, C1), 72.8 (s), 97.8 (s), 115.1 (s), 121.3 (s), 125.9 (d), 129.7 (d); IR (KBr, film) ν 3500–3100 (br, O–H), 3107 (m, =C–H), 2949 (s, C–H), 2226 (m, C≡C), 1506 (m), 1429 (s), 1348 (s), 1151 (m), 1056 (s), 939 (m), 863 (s), 708 (s), 607 (m); MS *m/z* (%) 247 ($[M+1]^+$ [^{81}Br], 10), 246 (M^+ [^{81}Br], 100), 245 ($[M+1]^+$ [^{79}Br], 17), 244 (M^+ [^{79}Br], 98), 201 (50), 199 (50), 190 (67), 188 (67), 177 (30), 175 (28), 165 (78), 147 (52), 137 (23), 135 (23), 134 (40), 123 (70), 122 (55), 121 (60), 97 (21); HRMS calcd for $C_9H_9{}^{81}BrOS$ 245.9537 and $C_9H_9{}^{79}BrOS$ 243.9557, found 245.9525 and 243.9547.

4.1.8. 6-(3-Bromothien-2-yl)hex-5-yn-1-ol (3e). In accordance to the general procedure for the Sonogashira coupling, treatment of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with hex-5-yn-1-ol **2e** (0.04 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 2.5 h at 60°C, afforded 0.06 g (56%) of alkynol **3e** as a yellow oil and 11 mg (25%) of a colorless solid (mp 50.9°C, CH_2Cl_2) identified as dodeca-5,7-diyn-1,12-diol (**4e**). *Data for* **3e**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.3–1.4 (m, 1H, OH), 1.6–1.8 (m, 4H, 2H2+2H3), 2.52 (t, *J*=6.5 Hz, 2H, 2H4), 3.71 (m, 2H, 2H1), 6.92 (d, *J*=5.3 Hz, 1H, H4′), 7.11 (d, *J*=5.3 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6 (t), 24.7 (t), 31.7 (t), 62.3 (t, C1), 72.6 (s), 98.3 (s), 115.0 (s), 121.4 (s), 125.8 (d), 129.7 (d); IR (KBr, film) ν 3600–3100 (br, O–H), 3107 (m, =C–H), 2939 (s, C–H), 2866 (m, C–H), 2226 (m, C≡C), 1429 (m), 1347 (m), 1060 (s), 863 (s), 709 (s); MS *m/z* (%) 260 (M^+ [^{81}Br], 34), 258 (M^+ [^{79}Br], 33), 242 (25), 240 (25), 216 (24), 214 (28), 212 (30), 203 (34), 201 (72), 199 (74), 179 (45), 177 (39), 175 (39), 151 (30), 148 (26), 147 (24), 135 (100), 123 (25), 122 (99), 120 (49); HRMS calcd for $C_{10}H_{11}{}^{81}BrOS$ 259.9693 and $C_{10}H_{11}{}^{79}BrOS$ 257.9714, found 259. 9697 and 257.9720.

4.1.9. 7-(3-Bromothien-2-yl)hept-6-yn-1-ol (3f). Following the general procedure described above, the reaction of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with hept-6-yn-1-ol **2f** (0.05 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 3 h at 80°C, afforded 0.02 g (20%) of alkynol **3f** as a yellow oil and 0.03 g (56%) of a colorless solid (mp 64.3°C, CH_2Cl_2) identified as tetradeca-6,8-diyn-1,14-diol (**4f**). *Data for* **3f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5–1.7 (m, 6H, 2H2+2H3+2H4), 2.47 (t, *J*=6.9 Hz, 2H, 2H5), 3.66 (t, *J*=6.3 Hz, 2H, 2H1), 6.90 (d, *J*=5.4 Hz, 1H, H4′), 7.09 (d, *J*=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8 (t), 25.0 (t), 28.1 (t), 32.2 (t), 62.8 (t, C1), 72.5 (s), 98.5 (s), 114.9 (s), 121.5 (s), 125.7 (d), 129.8 (d); IR (KBr, film) ν 3600–3100 (br, O–H), 3107 (w, =C–H), 2937 (s, C–H), 2861 (m, C–H), 2226 (w, C≡C), 1508 (w), 1428 (m), 1347 (m), 1150 (w), 1048 (m), 863 (s), 709 (s), 606 (m); MS *m/z* (%) 274 (M^+ [^{81}Br], 46), 272 (M^+ [^{79}Br], 46), 228 (41), 203 (38), 201 (97), 199 (98), 193 (66), 190 (44), 188 (42), 177 (59), 175 (58), 160 (42), 149 (39), 148 (41), 147 (81), 135 (71), 134 (59), 122 (100), 121 (52), 120 (67), 115 (29), 97 (61), 89 (28); HRMS calcd for $C_{11}H_{13}{}^{81}BrOS$ 273.9850 and $C_{11}H_{13}{}^{79}BrOS$ 271.9870, found 273.9837 and 271.9862. *Data for* **4f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (br s, 2H, 2×OH), 1.4–1.6 (m, 12H, 2H2+2H3+2H4+2H11+2H12+2H13), 2.25 (t, *J*=6.7 Hz, 4H, 2H5+2H10), 3.63 (t, *J*=6.0 Hz, 4H, 2H1+2H14); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 19.4 (t, 2×), 25.4 (t, 2×), 28.5 (t, 2×), 32.6 (t, 2×), 62.9 (t, 2×, C1+C14), 65.6 (s, 2×), 77.7 (s, 2×); IR (KBr, film) ν 3500–3100 (br, O–H), 2936 (s, C–H), 2860 (s, C–H), 1459 (m), 1053 (s), 627 (w); MS *m/z* (%) 222 (M^+, 0.3), 221 ($[M-1]^+$, 1), 150 (27), 149 (82), 135 (23), 131(39), 129 (34), 128 (26), 119 (36), 117 (84), 116 (26), 115 (48), 107 (27), 105 (78), 103 (33), 93 (31), 91 (100), 81 (32), 79 (77), 77 (68), 67 (51), 65 (26); HRMS calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1621.

4.1.10. 8-(3-Bromothien-2-yl)oct-7-yn-1-ol (3g). In accordance to the general procedure, treatment of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with oct-7-yn-1-ol

2g (0.05 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 3 h at 60°C, afforded 0.02 g (20%) of alkynol **3g** as a yellow oil and 0.03 g (55%) of a colorless solid (mp 44.5°C, CH_2Cl_2) identified as hexadeca-7,9-diyn-1,16-diol (**4g**). *Data for* **3g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.4–1.7 (m, 8H, 2H2+2H3+2H4+2H5), 2.46 (t, J=6.9 Hz, 2H, 2H6), 3.64 (t, J=6.6 Hz, 2H, 2H1), 6.90 (d, J=5.4 Hz, 1H, H4′), 7.09 (d, J=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7 (t), 25.2 (t), 28.3 (t), 28.5 (t), 32.6 (t), 62.9 (t, C1), 72.4 (s), 98.7 (s), 114.9 (s), 121.6 (s), 125.7 (d), 129.8 (d); IR (KBr, film) ν 3500–3100 (br, O–H), 3108 (w, =C–H), 2933 (s, C–H), 2858 (m, C–H), 2226 (w, C≡C), 1507 (w), 1428 (m), 1347 (m), 1150 (w), 1054 (m), 863 (s), 708 (s), 606 (w); MS *m/z* (%) 288 (M^+ [^{81}Br], 41), 286 (M^+ [^{79}Br], 40), 216 (75), 214 (75), 212 (27), 203 (52), 201 (81), 199 (86), 190 (28), 188 (27), 177 (29), 175 (29), 161 (39), 148 (55), 147 (55), 135 (86), 134 (29), 123 (25), 122 (100), 121 (38), 120 (48), 97 (28); HRMS calcd for $C_{12}H_{15}{}^{81}BrOS$ 288.0006 and $C_{12}H_{15}{}^{79}BrOS$ 286.0027, found 287.9999 and 286.0021. *Data for* **4g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (br s, 2H, 2×OH), 1.2–1.7 (m, 16H, 2H2+2H3+2H4+2H5+2H12+2H13+2H14+2H15), 2.24 (t, J=6.8 Hz, 4H, 2H6+2H11), 3.62 (t, J=6.3 Hz, 4H, 2H1+2H16); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 19.4 (t, 2×), 25.6 (t, 2×), 28.7 (t, 2×), 29.0 (t, 2×), 33.1 (t, 2×), 63.0 (t, 2×, C1+C16), 65.5 (s, 2×), 77.8 (s, 2×); IR (KBr, film) ν 3500–3100 (br, O–H), 2934 (s, C–H), 2859 (s, C–H), 1460 (m), 1427 (m), 1055 (m), 725 (w), 542 (w); MS (FAB$^+$) *m/z* (%) 252 ($[M+2]^+$, 12), 251 ($[M+1]^+$, 71); HRMS (FAB$^+$) ($[M+H]^+$) calcd for $C_{16}H_{27}O_2$ 251.2011, found 251.2011.

4.1.11. 9-(3-Bromothien-2-yl)non-8-yn-1-ol (3h). According to the general procedure for the Sonogashira coupling, the reaction of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with non-8-yn-1-ol **2h** (0.06 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 3 h at 60°C, provided 0.05 g (42%) of compound **3h** as a yellow oil and 0.03 g (43%) of a colorless solid (mp 66.6°C, CH_2Cl_2) identified as octadeca-8,10-diyn-1,18-diol (**4h**). *Data for* **3h**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.2–1.7 (m, 10H, 2H2+2H3+2H4+2H5+2H6), 2.44 (t, J=7.0 Hz, 2H, 2H7), 3.63 (t, J=6.6 Hz, 2H, 2H1), 6.90 (d, J=5.4 Hz, 1H, H4′), 7.09 (d, J=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7 (t), 25.6 (t), 28.2 (t), 28.7 (t), 28.8 (t), 32.7 (t), 63.0 (t, C1), 72.3 (s), 98.8 (s), 114.8 (s), 121.6 (s), 125.6 (d), 129.7 (d); IR (KBr, film) ν 3500–3100 (br, O–H), 3107 (w, =C–H), 2932 (s, C–H), 2856 (s, C–H), 2226 (w, C≡C), 1507 (w), 1429 (m), 1348 (m), 1150 (w), 1057 (m), 863 (s), 707 (s), 607 (m); MS *m/z* (%) 302 (M^+ [^{81}Br], 37), 300 (M^+ [^{79}Br], 36), 229 (27), 227 (27), 216 (55), 214 (53), 203 (57), 201 (68), 199 (71), 190 (26), 188 (24), 177 (28), 175 (29), 162 (25), 161 (29), 148 (50), 147 (45), 135 (90), 134 (32), 123 (25), 122 (100), 121 (39), 120 (38); HRMS calcd for $C_{13}H_{17}{}^{81}BrOS$ 302.0163 and $C_{13}H_{17}{}^{79}BrOS$ 300.0183, found 302.0150 and 300.0173. *Data for* **4h**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.2–1.6 (m, 20H, 2H2+2H3+2H4+2H5+2H6+2H13+2H14+2H15+2H16+2H17), 2.23 (t, J=6.9 Hz, 4H, 2H7+2H12), 3.62 (t, J=6.3 Hz, 4H, 2H1+2H18); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 19.4 (t, 2×), 26.0 (t, 2×), 28.7 (t, 2×), 29.1 (t, 2×), 29.2 (t, 2×), 33.2 (t, 2×), 63.1 (t, 2×, C1+C18), 65.5 (s, 2×), 77.9 (s, 2×); IR (KBr, film) ν 3500–3100 (br, O–H), 2931 (s, C–H), 2853 (s, C–H), 1464 (m), 1352 (w), 1061 (m), 1021 (w), 983 (w), 726 (w), 623 (w); MS *m/z* (%) 278 (M^+, 3), 177 (21), 145 (32), 133 (30), 131 (50), 119 (63), 117 (52), 107 (24), 106 (25), 105 (62), 95 (25), 93 (48), 92 (33), 91 (100), 81 (55), 80 (34), 79 (62), 78 (30), 77 (34), 67 (50); HRMS calcd for $C_{18}H_{30}O_2$ 278.2246, found 278.2237.

4.1.12. *tert*-Butyldimethylsilyl 6-(3-bromothien-2-yl)hex-5-yn-1-yl ether (3i). Following the general procedure described above, treatment of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with *tert*-butyldimethylsilyl hex-5-yn-1-yl ether **2i** (0.10 g, 0.45 mmol), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 3 h at 60°C, afforded, after purification by chromatography (SiO_2, 85:15–70:30 hexane/CH_2Cl_2), 0.06 g (42%) of compound **3i** as a yellow oil and 0.04 g (40%) of a colorless oil identified as 1,12-bis(*tert*-butyldimethylsilyloxy)dodeca-5,7-diyne (**4i**). *Data for* **3i**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.92 (s, 9H, $SiC(CH_3)_3$), 1.7–1.8 (m, 4H, 2H2+2H3), 2.52 (t, J=6.6 Hz, 2H, 2H4), 3.69 (t, J=6.0 Hz, 2H, 2H1), 6.93 (d, J=5.4 Hz, 1H, H4′), 7.12 (d, J=5.4 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.3 (q, 2×, $Si(CH_3)_2$), 18.3 (s, $SiC(CH_3)_3$), 19.6 (t), 24.9 (t), 25.9 (q, 3×, $SiC(CH_3)_3$), 31.8 (t), 62.6 (t, C1), 72.4 (s), 98.6 (s), 114.9 (s), 121.6 (s), 125.7 (d), 129.7 (d); IR (NaCl, film) ν 3108 (w, =C–H), 2952 (s, C–H), 2929 (s, C–H), 2857 (s, C–H), 2229 (w, C≡C), 1471 (m), 1254 (s), 1106 (s), 836 (s), 776 (s); MS *m/z* (%) 318 ($[M+1\text{-}t\text{Bu}]^+$ [^{81}Br], 19), 317 ($[M-t\text{Bu}]^+$ [^{81}Br], 100), 316 ($[M+1\text{-}t\text{Bu}]^+$ [^{79}Br], 19), 315 ($[M-t\text{Bu}]^+$ [^{79}Br], 93), 241 (51), 162 (24), 75 (67); HRMS ($[M-t\text{Bu}]^+$) calcd for $C_{12}H_{16}{}^{81}BrOSSi$ 316.9854 and $C_{12}H_{16}{}^{79}BrOSSi$ 314.9874, found 316.9839 and 314.9883. *Data for* **4i**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.02 (s, 12H, 2×$Si(CH_3)_2$), 0.86 (s, 18H, 2×Si–*t*Bu), 1.5–1.6 (m, 8H, 2H2+2H3+2H10+2H11), 2.25 (t, J=6.5 Hz, 4H, 2H4+2H9), 3.59 (t, J=5.9 Hz, 4H, 2H1+2H12); ^{13}C NMR (100 MHz, CD_2Cl_2) δ −5.2 (q, 4×, 2×$Si(CH_3)_2$), 18.6 (s, 2×, 2×$SiC(CH_3)_3$), 19.3 (t, 2×), 25.3 (t, 2×), 26.1 (q, 6×, 2×$SiC(CH_3)_3$), 32.3 (t, 2×), 62.8 (t, 2×, C1+C12), 65.7 (s, 2×), 77.8 (s, 2×); IR (KBr, film) ν 2954 (s, C–H), 2932 (s, C–H), 2859 (s, C–H), 1469 (m), 1254 (s), 1107 (s), 837 (s), 776 (s); MS *m/z* (%) 423 ($[M+1]^+$, 1), 422 (M^+, 1), 365 (42), 233 (28), 159 (52), 148 (21), 147 (100), 131 (34), 117 (32), 91 (31), 75 (80), 73 (75); HRMS calcd for $C_{24}H_{46}O_2Si_2$ 422.3036, found 422.3048.

4.1.13. 3-Bromo-2-(hex-1-yn-1-yl)thiophene (3j). According to the general procedure for the Sonogashira reaction, treatment of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) with 1-hexyne **2j** (0.04 g, 0.45 mmol) in *i*Pr_2NH (2 mL), in the presence of $Pd(PPh_3)_2Cl_2$ (1.2 mg, 0.002 mmol), PPh_3 (0.6 mg, 0.002 mmol) and CuI (0.6 mg, 0.003 mmol), for 2 h at 84°C, afforded an inseparable mixture of 2,3-dibromothiophene **1**, C2-substituted product **3j** and alkyne dimer **4j**. Integration of its ^{1}H NMR spectrum showed a 4:1:2 **1/3j/4j** ratio.

4.1.14. (2*E*,4*E*)-5-(3-Bromothien-2-yl)-3-methylpenta-2,4-dien-1-ol (7a). *Procedure A for the Stille reaction*. To a solution of $Pd_2(dba)_3$ (11 mg, 0.01 mmol) in NMP (1 mL)

was added, in one portion, $AsPh_3$ (25 mg, 0.08 mmol). Degassing of the solution was accomplished by bubbling an Ar current through the mixture for 5 min. A previously degassed solution of 2,3-dibromothiophene **1** (0.10 g, 0.41 mmol) in NMP (1 mL) was then added, dropwise. After stirring at 25°C for 10 min, a degassed solution of (2*E*,4*E*)-5-(tri-*n*-butylstannyl)-3-methylpenta-2,4-dien-1-ol **5** (0.24 g, 0.62 mmol) in NMP (1 mL) was added and the final mixture was heated to 45°C for 90 min. After cooling down to 25°C, a KF saturated solution (4 mL) was added and the mixture was stirred for 30 min. It was then extracted with TBME (3×5 mL). The combined organic extracts were washed with H_2O (2×15 mL) and KF saturated solution (15 mL), dried (Na_2SO_4) and evaporated. Purification of the residue by chromatography (SiO_2, 75:25–50:50 hexane/AcOEt) afforded 0.07 g (70%) of a yellow solid (mp 85.3°C, CH_2Cl_2/hexane) identified as (2*E*,4*E*)-5-(3-bromothien-2-yl)-3-methylpenta-2,4-dien-1-ol (**7a**) and 0.02 g of a mixture which was further purified by HPLC (Waters Spherisorb® S5NH$_2$, 10×250 mm; 97:3 CH_2Cl_2/MeOH, 4.4 mL/min, 13 min) to afford 10 mg (9%) of a yellow solid (mp 131.4°C, CH_2C_2) identified as 2,3-bis[(1*E*,3*E*)-3-methylpenta-1,3-dien-5-ol-1-yl]thiophene (**8a**). *Data for* **7a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J=5.6 Hz, 1H, OH), 1.89 (s, 3H, C3–CH_3), 4.31 (app. t, J=6.2 Hz, 2H, 2H1), 5.79 (t, J=6.8 Hz, 1H, H2), 6.64 (d, J_{AB}=16.0 Hz, 1H, H4 or H5), 6.69 (d, J_{AB}=16.0 Hz, 1H, H5 or H4), 6.91 (d, J=5.3 Hz, 1H, H4′), 7.09 (d, J=5.3 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5 (q, C3–CH_3), 59.4 (t, C1), 110.5 (s), 119.5 (d), 123.7 (d), 130.7 (d), 132.0 (d), 134.4 (d), 135.8 (s), 137.2 (s); IR (KBr, film) ν 3500–3100 (br, O–H), 2920 (m, C–H), 1433 (m), 997 (m), 945 (s), 875 (m), 704 (s); MS *m*/*z* (%) 260 (M$^+$ [^{81}Br], 49), 258 (M$^+$ [^{79}Br], 50), 190 (35), 188 (34), 179 (33), 177 (49), 175 (47), 149 (l00), 136 (43), 135 (36), 134 (34); HRMS calcd for $C_{10}H_{11}{}^{81}BrOS$ 259.9693 and $C_{10}H_{11}{}^{79}BrOS$ 257.9714, found 259.9686 and 257.9717. *Data for* **8a**: ^{1}H NMR (400 MHz, CD_3COCD_3) δ 1.82 (s, 6H, C3′–CH_3+C3″–CH_3), 3.6 (m, 2H, 2×OH), 4.20 (t, J=6.0 Hz, 4H, 2H5′+2H5″), 5.73 (t, J=6.4 Hz, 2H, H4′+H4″), 6.58 (d, J=15.7 Hz, 1H, H2′ or H1′ or H2″ or H1″), 6.72 (d, J_{AB}=16.1 Hz, 1H, H2′ or H1′ or H2 or H1″), 6.75 (d, J_{AB}=16.1 Hz, 1H, H2′ or H1′ or H2″ or H1″), 6.92 (d, J=15.7 Hz, 1H, H2′ or H1′ or H2″ or H1″), 7.18 (d, J=5.4 Hz, 1H, H4), 7.24 (d, J=5.4 Hz, 1H, H5); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 12.6 (q), 12.7 (q), 59.4 (t), 59.5 (t), 119.3 (d), 120.2 (d), 124.6 (d), 126.9 (d), 134.4 (d, 2×), 134.7 (d), 135.1 (s), 135.2 (d), 135.3 (s), 137.8 (s), 138.8 (s); IR (KBr, film) ν 3500–3100 (br, O–H), 2923 (m, C–H), 2854 (m, C–H), 1249 (w), 995 (m), 952 (m), 721 (w); MS *m*/*z* (%) 277 ([M+1]$^+$, 17), 276 (M$^+$, 100), 245 (53), 227 (24), 187 (29), 175 (27), 161 (47), 149 (22), 148 (28), 135 (21); HRMS calcd for $C_{16}H_{20}O_2S$ 276.1184, found 276.1178.

4.1.15. 2-(3-Bromothien-2-yl)furane (7b). *Procedure B for the Stille reaction*. To a stirred solution of 2,3-dibromothiophene **1** (50 mg, 0.21 mmol) and $Pd_2(dba)_3$ (2.8 mg, 0.003 mmol) in dioxane (1 mL) was added, via cannula, a solution of P*t*Bu$_3$ (2.5 mg, 0.01 mmol) in dioxane (1 mL). After stirring at 25°C for 10 min, 2-(tri-*n*-butylstannyl)furane **6** (0.08 g, 0.23 mmol) in dioxane (1 mL) was added, followed by CsF (0.07 g, 0.45 mmol). The reaction mixture was stirred at 25°C for 2 h. It was then diluted with TBME and filtered through a plug of silica gel. After evaporation of the solvent, the residue was purified by chromatography (SiO_2, hexane), to yield 0.03 g (72%) of compound **7b** as a colorless oil and 5 mg (11%) of a colorless oil identified as 1,3-bis(fur-2-yl)thiophene (**8b**). *Data for* **7b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (dd, J=3.5, 1.8 Hz, 1H, H4), 7.02 (d, J=5.3 Hz,1H, H4′), 7.08 (dd, J=3.5, 0.5 Hz, 1H, H3), 7.22 (d, J=5.3 Hz, 1H, H5′), 7.46 (dd, J=1.8, 0.5 Hz, 1H, H5); ^{13}C NMR (100 MHz, $CDCl_3$) δ 106.0 (s), 107.7 (d), 111.7 (d), 124.2 (d), 128.9 (s), 131.5 (d), 141.8 (d), 147.6 (s); IR (KBr, film) ν 3110 (m, =C–H), 2926 (m, C–H), 1487 (s), 1344 (m), 865 (s), 735 (s), 708 (s); MS *m*/*z* (%) 231 ([M+1]$^+$ [^{81}Br], 9), 230 (M$^+$ [^{81}Br], 100), 229 ([M+1]$^+$ [^{79}Br], 10), 228 (M$^+$ [^{79}Br], 98), 201 (21), 199 (21), 191 (24), 189 (23), 121 (81); HRMS calcd for $C_8H_5{}^{81}BrOS$ 229.9224 and $C_8H_5{}^{79}BrOS$ 227.9244, found 229.9218 and 227.9242. *Data for* **8b**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 6.4–6.5 (m, 3H, H4′+H3″+H4″), 6.62 (dd, J=3.3, 0.6 Hz, 1H, H3′), 7.28 (d, J=5.3 Hz, 1H, H4 or H5), 7.31 (d, J=5.3 Hz, 1H, H5 or H4), 7.46 (dd, J=1.8, 0.6 Hz, 1H, H5″ or H5′), 7.48 (dd, J=1.6, 0.6 Hz, 1H, H5′ or H5″); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 108.1 (d), 109.2 (d), 111.7 (d), 112.1 (d), 125.3 (d), 127.7 (s), 128.3 (s), 128.4 (d), 141.9 (d), 142.6 (d), 148.1 (s), 150.2 (s); IR (KBr, film) ν 3115 (w, =C–H), 1484 (w), 1019 (m), 855 (m), 734 (s); MS *m*/*z* (%) 217 ([M+1]$^+$, 15), 216 (M$^+$, 100), 187 (40), 115 (22), 68 (29); HRMS calcd for $C_{12}H_8O_2S$ 216.0245, found 216.0234.

4.1.16. 3-Bromo-2-phenylthiophene (12a). *Procedure A for the Suzuki reaction*. To a stirred solution of 2,3-dibromothiophene **1** (0.20 g, 0.83 mmol) and Pd(PPh$_3$)$_4$ (0.09 g, 0.07 mmol) in dioxane (10 mL) were added phenylboronic acid **10** (0.11 g, 0.91 mmol) and 2 M Na_2CO_3 (1.7 mL, 3.31 mmol). The mixture was heated to 100°C for 4 h. After cooling down to 25°C, it was diluted with TBME, poured into H_2O and extracted with TBME (3×). The combined organic extracts were washed with a NaCl saturated solution (3×), dried (Na_2SO_4) and evaporated. Purification by chromatography (SiO_2, hexane) afforded 0.16 g (81%) of compound **12a** as a colorless oil, and 4 mg (2%) of a colorless solid (mp 83.7°C, hexane) identified as 2,3-diphenylthiophene (**13a**). *Data for* **12a**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.07 (d, J=5.3 Hz, 1H, H4), 7.32 (d, J=5.3 Hz, 1H, H5), 7.4–7.5 (m, 3H, ArH), 7.6–7.7 (m, 2H, ArH); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 107.8 (s, C3), 125.6 (d), 128.6 (d), 128.9 (d, 2×), 129.3 (d, 2×), 131.9 (d), 133.1 (s), 138.5 (s); IR (KBr, film) ν 3108 (m, =C–H), 2924 (m, C–H), 1484 (m), 1445 (m), 1147 (m), 864 (s), 757 (s), 692 (s); MS *m*/*z* (%) 241 ([M+1]$^+$ [^{81}Br], 11), 240 (M$^+$ [^{81}Br], 100), 239 ([M+1]$^+$ [^{79}Br], 11), 238 (M$^+$ [^{79}Br], 96), 115 (68), 114 (10); HRMS calcd for $C_{10}H_7{}^{81}BrS$ 239.9431 and $C_{10}H_7{}^{79}BrS$ 237.9452, found 239.9425 and 237.9443.

4.1.17. (5*E*)-6-(3-Bromothien-2-yl)hex-5-en-1-ol (12b). *Procedure B for the Suzuki reaction*. Argon was bubbled through a solution of boronic acid **11** (0.07 g, 0.52 mmol) in THF (1 mL) for 10 min. A previously degassed 10% aqueous TlOH solution (2.3 mL, 1.05 mmol) was then added. After stirring at 25°C for 10 min, this mixture was slowly added, via cannula, over a degassed solution of 2,3-dibromothiophene **1** (50 mg, 0.21 mmol) and

$Pd(PPh_3)_4$ (24 mg, 0.02 mmol) in THF (1 mL). The reaction mixture was stirred at 25°C for 6 h. It was then diluted with AcOEt and filtered through a plug of Celite®. The filtrate was dried (Na_2SO_4) and evaporated. Purification of the residue by chromatography (70:30–50:50 hexane/AcOEt) afforded 0.03 g (51%) of **12b** as a yellow oil and 11 mg (21%) of a colorless solid (mp 68.4°C, hexane/AcOEt) identified as (5*E*,7*E*)-dodeca-5,7-dien-1,12-diol (**14b**).[34] *Data for* **12b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.3 (br s, 1H, OH), 1.5–1.7 (m, 4H, 2H2+2H3), 2.2–2.3 (m, 2H, 2H4), 3.66 (t, J=6.3 Hz, 2H, 2H1), 6.11 (dt, J=15.8, 7.0 Hz, 1H, H5), 6.54 (d, J=15.8 Hz, 1H, H6), 6.88 (d, J=5.3 Hz, 1H, H4′), 7.04 (d, J=5.3 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2 (t), 32.2 (t), 32.7 (t), 62.7 (t, C1), 108.7 (s, C3′), 121.9 (d), 122.9 (d), 130.4 (d), 132.9 (d), 137.1 (s, C2′); IR (KBr, film) ν 3500–3100 (br, O–H), 2933 (s, C–H), 2860 (s, C–H), 1436 (m), 1347 (w), 1060 (m), 955 (s), 868 (s), 699 (s); MS *m/z* (%) 262 (M^+ [^{81}Br], 19), 260 (M^+ [^{79}Br], 19), 192 (34), 191 (51), 190 (30), 189 (47), 181 (32), 177 (33), 175 (32), 163 (18), 135 (44), 122 (100), 97 (29), 85 (63); HRMS calcd for $C_{10}H_{13}{}^{81}BrOS$ 261.9850 and $C_{10}H_{13}{}^{79}BrOS$ 259.9870, found 261.9855 and 259.9881. *Data for* **14b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.4–1.6 (m, 8H, 2H2+2H3+2H10+2H11), 2.07 (app. q, J=7.1 Hz, 4H, 2H4+2H9), 3.62 (t, J=6.5 Hz, 4H, 2H1+2H12), 5.5–5.6 (m, 2H, H5+H8), 5.9–6.0 (m, 2H, H6+H7); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.4 (t, 2×), 32.2 (t, 4×), 62.8 (t, 2×, C1+C12), 130.6 (d, 2×), 132.0 (d, 2×); IR (KBr, film) ν 3500–3100 (br, O–H), 3014 (m, =C–H), 2933 (s, C–H), 1434 (w), 1060 (m), 987 (s); MS *m/z* (%) 198 (M^+, 3), 180 (42), 121 (25), 107 (21), 98 (51), 97 (23), 95 (47), 94 (35), 93 (57), 91 (40), 84 (25), 82 (27), 81 (50), 80 (60), 79 (100), 77 (31), 68 (27), 67 (42); HRMS calcd for $C_{12}H_{22}O$ 198.1620, found 198.1625.

4.1.18. 3-Bromo-2-phenylthiophene (12a). *Procedure C for the Suzuki reaction*. The mixture of $Pd(OAc)_2$ (0.5 mg, 0.002 mmol), 2-(di-*tert*-butylphosphino)biphenyl **15** (1.2 mg, 0.004 mmol), phenyl boronic acid **10** (38 mg, 0.31 mmol) and K_3PO_4 (0.09 g, 0.41 mmol) was degassed by means of 3 vacuum-Ar cycles. To this mixture was added a previously degassed solution of 2,3-dibromothiophene **1** (50 mg, 0.21 mmol) in toluene (1 mL) and the final solution was heated to 100°C for 4 h. After cooling down to 25°C, TBME was added, the mixture was poured into a 1 M NaOH solution and it was extracted with TBME (3×5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Purification by chromatography (SiO_2, hexane) afforded 0.02 g (40%) of **12a** and 4 mg (8%) of **13a**.

4.1.19. (5*E*)-6-(3-Bromothien-2-yl)hex-5-en-1-ol (12b). *Procedure D for the Suzuki reaction*. The mixture of $Pd(OAc)_2$ (0.5 mg, 0.002 mmol), 2-(di-*tert*-butylphosphino)-biphenyl **15** (1.2 mg, 0.004 mmol), boronic acid **11** (75 mg, 0.52 mmol) and KF (0.04 g, 0.62 mmol) was degassed by means of three vacuum-Ar cycles. To this mixture was added a previously degassed solution of 2,3-dibromothiophene **1** (50 mg, 0.21 mmol) in dioxane (1 mL) and the final solution was heated to 90°C for 5 h. After cooling down to 25°C, AcOEt was added, the mixture was poured into a 1 M NaOH solution and it was extracted with AcOEt (3×5 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated. Purification by chromatography (SiO_2, 70:30–40:60 hexane/AcOEt) afforded 0.03 g (64%) of **12b** and 14 mg of a mixture which was further purified by HPLC (Waters Spherisorb® $S5NH_2$, 10×250 mm; 97:3 CH_2Cl_2/MeOH, 4.4 mL/min, 18 min) to afford 7 mg (12%) of a yellow oil identified as 2,3-bis[(1*E*)hex-1-en-6-ol-1-yl]-thiophene (**13b**). *Data for* **13b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.5–1.6 (m, 8H, 2H4′+2H5′+2H4″+2H5″), 2.22 (qd, J=7.1, 1.2 Hz, 4H, 2H3′+2H3″), 3.66 (t, J=6.4 Hz, 4H, 2H6′+2H6″), 5.99 (dtd, J=15.7, 7.0, 2.0 Hz, 2H, H2′+H2″), 6.46 (d, J=15.7 Hz, 1H, H1′ or H1″), 6.62 (d, J=15.7 Hz, 1H, H1″ or H1′), 6.96 (d, J=5.3 Hz, 1H, H4), 7.04 (d, J=5.3 Hz, 1H, H5); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3 (t), 25.4 (t), 32.0 (t, 2×), 32.7 (t), 32.8 (t), 62.3 (t), 62.4 (t), 121.3 (d), 122.4 (d, 2×), 125.6 (d), 131.0 (d), 131.1 (d), 135.1 (s), 136.5 (s); IR (KBr, film) ν 3600–3100 (br, O–H), 3024 (w, =C–H), 2933 (s, C–H), 2861 (s, C–H), 1657 (m), 1434 (m), 1063 (s), 958 (s), 718 (m); MS *m/z* (%) 280 (M^+, 23), 210 (25), 148 (20), 147 (51), 137 (100), 135 (36), 123 (21), 85 (29), 69 (28); HRMS calcd for $C_{16}H_{24}O_2S$ 280.1497, found 280.1502.

4.1.20. *tert*-Butyldimethylsilyl 6-(thien-2-yl)hex-5-yn-1-yl ether (16). To a cooled (0°C) solution of *tert*-butyldimethylsilyl 6-(3-bromothien-2-yl)hex-5-yn-1-yl ether **3i** (50 mg, 0.13 mmol) in THF (1 mL) was added dropwise *sec*-BuLi (0.12 mL, 1.3 M in cyclohexane, 0.16 mmol). After stirring at 0°C for 30 min, MeOH (0.05 mL, 1.33 mmol) was added and the resulting mixture was stirred at 25°C for 30 min. Water was then added and the mixture was extracted with Et_2O (3×). The combined organic layers were washed with H_2O (3×), dried (Na_2SO_4) and evaporated. Purification by chromatography (SiO_2–C_{18}, 100% CH_3CN) afforded 35 mg (92%) of **16** as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H, $Si(CH_3)_2$), 0.92 (s, 9H, *t*Bu), 1.6–1.7 (m, 4H, 2H2+2H3), 2.47 (t, J=6.6 Hz, 2H, 2H4), 3.68 (t, J=5.7 Hz, 2H, 2H1), 6.94 (dd, J=4.9, 3.6 Hz, 1H, H4′), 7.12 (d, J=3.6 Hz, 1H, H3′), 7.17 (d, J=4.9 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ −5.3 (q, 2×, $Si(CH_3)_2$), 18.3 (s, $SiC(CH_3)_3$), 19.5 (t), 25.0 (t), 25.9 (q, 3×, $SiC(CH_3)_3$), 32.0 (t), 62.6 (t, C1), 73.8 (s), 94.2 (s), 124.1 (s), 125.8 (d), 126.7 (d), 130.9 (d); IR (KBr, film) ν 2929 (s, C–H), 2857 (s, C–H), 1361 (m), 1256 (s), 1107 (s), 836 (s), 775 (s), 696 (s); MS *m/z* (%) 238 ([M+1-*t*Bu]$^+$, 19), 237 ([M−*t*Bu]$^+$, 90), 171 (25), 164 (20), 163 (100), 121 (19), 97 (14), 75 (36); HRMS calcd for $C_{16}H_{26}OSSi$ 294.1474, found 294.1471.

4.1.21. 2-(Hex-1-yn-6-ol-1-yl)-3-[(1*E*,3*E*)-3-methylpenta-1,3-dien-5-ol-1-yl]thiophene (17). In accordance to procedure B for the Stille coupling, the reaction of 6-(3-bromothien-2-yl)hex-5-yn-1-ol **3e** (0.05 g, 0.19 mmol) with (2*E*,4*E*)-5-(tri-*n*-butylstannyl)-3-methylpenta-2,4-dien-1-ol **5** (0.11 g, 0.29 mmol), in the presence of $Pd_2(dba)_3$ (2.6 mg, 0.003 mmol), P*t*Bu_3 (2.3 mg, 0.01 mmol) and CsF (0.06 g, 0.42 mmol), for 2 h at 80°C, afforded, after purification by chromatography (Al_2O_3, CH_2Cl_2–97:3 CH_2Cl_2/MeOH), 0.04 g (76%) of thiophene **17** as a yellow solid (mp 66.5°C, CH_2Cl_2) and 7 mg (20%) of a yellow oil identified as 6-(thien-2-yl)hex-5-yn-1-ol (**18**).[35] *Data for* **17**: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 1.5–1.8 (m, 6H, 2H4′+2H5′+2×OH), 1.89 (s, 3H, C3″–CH_3), 2.55 (t, J=6.6 Hz, 2H, 2H3′), 3.66 (t, J=6.0 Hz, 2H, 2H6′), 4.30 (d, J=6.7 Hz, 2H, 2H5″), 5.79 (t, J=6.7 Hz, 1H, H4″), 6.73 (d, J_{AB}=

16.2 Hz, 1H, H1″ or H2″), 6.81 (d, J_{AB}=16.2 Hz, 1H, H2″ or H1″), 7.11 (d, J=5.4 Hz, 1H, H4 or H5), 7.14 (d, J=5.4 Hz, 1H, H5 or H4); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 12.6 (q, C3″–CH_3), 20.0 (t), 25.4 (t), 32.3 (t), 59.7 (t), 62.6 (t), 73.7 (s), 99.1 (s), 121.4 (d), 124.8 (d), 125.7 (d), 132.2 (d), 134.4 (d), 136.2 (s, 2×), 142.6 (s); IR (KBr, film) ν 3600–3100 (br, O–H), 3106 (w, =C–H), 2939 (s, C–H), 2219 (w, C≡C), 1711 (m), 1663 (m), 1429 (m), 1248 (m), 1060 (m), 833 (m), 755 (s); MS *m/z* (%) 277 ([M+1]$^+$, 19), 276 (M$^+$, 100), 245 (68), 187 (57), 185 (49), 184 (39), 175 (37), 171 (47), 161 (58), 147 (46); HRMS calcd for $C_{16}H_{20}O_2S$ 276.1184, found 276.1180. *Data for* **18**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.6–1.7 (m, 4H, 2H2+2H3), 2.45 (t, J=6.6 Hz, 2H, 2H4), 3.68 (t, J=5.9 Hz, 2H, 2H1), 6.91 (dd, J=5.1, 3.6 Hz, 1H, H4′), 7.09 (d, J=3.6 Hz, 1H, H3′), 7.15 (d, J=5.1 Hz, 1H, H5′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4 (t), 24.8 (t), 31.8 (t), 62.3 (t, C1), 74.0 (s), 93.9 (s), 124.0 (s, C2′), 125.9 (d), 126.7 (d), 131.0 (d); IR (KBr, film) ν 3500–3100 (br, O–H), 3106 (w, =C–H), 2939 (s, C–H), 2866 (s, C–H), 2224 (w, C≡C), 1428 (m), 1239 (w), 1190 (m), 1061 (s), 845 (m), 700 (s); MS *m/z* (%) 180 (M$^+$, 43), 162 (33), 136 (37), 135 (57), 134 (48), 124 (31), 123 (91), 121 (100), 97 (46), 77 (26); HRMS calcd for $C_{10}H_{12}OS$ 180.0609, found 180.0604.

4.1.22. 2-Phenyl-3-[(1*E*,3*E*)-3-methylpenta-1,3-dien-5-ol-1-yl]thiophene (19). According to procedure B for the Stille reaction, treatment of 3-bromo-2-phenylthiophene **12a** (0.05 g, 0.21 mmol) with (2*E*,4*E*)-5-(tri-*n*-butylstannyl)-3-methylpenta-2,4-dien-1-ol **5** (0.12 g, 0.31 mmol), in the presence of $Pd_2(dba)_3$ (2.9 mg, 0.003 mmol), P*t*Bu$_3$ (2.5 mg, 0.01 mmol) and CsF (0.07 g, 0.46 mmol), for 2 h at 80°C, afforded, after purification by chromatography (SiO_2, hexane–70:30 hexane/AcOEt), 0.04 g (80%) of thiophene **19** as a yellow oil and 5 mg (15%) of a colorless solid (mp 36.6°C, EtOH/H_2O) identified as 2-phenylthiophene (**20**).[¶] *Data for* **19**: ^{1}H NMR (400 MHz, CD_3COCD_3) δ 1.75 (s, 3H, C3′–CH_3), 3.66 (t, J=5.3 Hz, 1H, OH), 4.25 (t, J=5.9 Hz, 2H, 2H5′), 5.79 (t, J=6.4 Hz, 1H, H4′), 6.64 (d, J=16.1 Hz, 1H, H1′ or H2′), 6.84 (d, J=16.1 Hz, 1H, H2′ or H1′), 7.4–7.5 (m, 5H, ArH), 7.43 (d, J_{AB}=5.4 Hz, 1H, H4 or H5), 7.44 (d, J_{AB}=5.4 Hz, 1H, H5 or H4); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 12.5 (q, C3′–CH_3), 59.4 (t, C5′), 121.3 (d), 125.7 (d), 127.0 (d), 128.7 (d), 129.7 (d, 2×), 130.2 (d, 2×), 134.1 (d), 135.1 (s), 135.2 (s), 135.3 (d), 136.4 (s), 140.0 (s); IR (KBr, film) ν 3600–3100 (br, O–H), 2924 (s, C–H), 1599 (m), 1491 (m), 1445 (m), 1386 (w), 1246 (w), 1076 (w), 1002 (m), 960 (m), 835 (m), 762 (s), 700 (m), 646 (m); MS *m/z* (%) 257 ([M+1]$^+$, 8), 256 (M$^+$, 45), 226 (18), 225 (100), 213 (16), 187 (16), 186 (17), 185 (43), 184 (26), 173 (27), 171 (19); HRMS calcd for $C_{16}H_{16}OS$ 256.0922, found 256.0917.

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[¶] 2-Phenylthiophene is commercially available.

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