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Double C–H bond functionalization for C–C coupling at the β-position of thiophenes using palladium-catalyzed 1,4-migration associated with direct arylation†

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The functionalization of C–H bonds at β-positions of 5-membered ring heteroarenes such as thiophene is generally more challenging than at α-positions. By using Pd-catalyzed 1,4-migration associated with direct arylation, under appropriate conditions, the functionalization of such thienyl β-positions of 2-arylthiophenes is possible. The oxidative addition of 2-(2-bromoaryl)thiophenes to palladium followed by Pd 1,4-migration activates these β-positions. Then, Pd-catalyzed direct coupling with heteroarenes provides β-heteroarylated 2-arylthiophene derivatives. In the course of this coupling reaction, a new C–C bond arises from the functionalization of two C–H bonds. Conversely, the Suzuki reaction using such 2-(2-bromoaryl)thiophenes provides 1,2-diheteroaryl-substituted benzene derivatives. These regiodivergent heteroarylations tolerate a range of substituents on the benzene ring and also several heteroarenes and provide a new route to π-extended polycyclic heteroaromatics. Moreover, these procedures employ easily available air-stable catalysts and inexpensive bases.

Introduction

When specific C–H bonds of organic molecules can be directly functionalized *via* catalytic reactions, it often provides simple synthetic methods.[1] Metal-catalyzed C–H bond activation/functionalization of heteroarenes, reported by Ohta *et al.* 1990, now represents one of the most effective methods for the preparation of heteroarylated arenes.[2] For such coupling reactions, initially in most cases, only the "most reactive" C–H bond of (hetero)arenes could be functionalized.[3–7] Nevertheless, the C–H bond functionalization methodology will only be really synthetically useful when it will be possible to activate a specific C–H bond on the molecules. Therefore, the discovery of conditions allowing the regioselective functionalization of several bonds of the same molecule, also called regiodivergent functionalization, is a very important aspect of the current research on metal-catalyzed reactions.

So far, the Pd-catalyzed reactions such as Suzuki coupling of heteroarylboronic acids with thiophenes bearing a 2-halobenzene substituent selectively lead to 1,2-diheteroarylated benzene derivatives (Scheme 1a).[8] On the other hand, the C3-heteroarylation of 2-aryl-3-halothiophenes for the access to the corresponding heteroaryl-substituted thiophene derivatives *via* metal-catalyzed reactions has been rarely described (Scheme 1b).[9,10] This might be due to the tedious multi-step route to many 3-halothiophene derivatives.[11] To the best of our knowledge, the synthesis of 2-aryl-3-heteroarylthiophenes from 2-(2-bromoaryl)thiophenes has not been reported so far (Scheme 1c, bottom). We have recently reported that in the course of the heteroarylation of 1,2-dihalobenzenes by thiophenes, a partial Pd 1,4-migration occurred[12,13] in some cases, leading to a mixture of 1,2-diheteroarylated benzenes and also to aryl-substituted biheteroarenes such as 2′-aryl-2,3′-bithiophenes.[14] This Pd 1,4-migration on thiophene derivatives provides an appealing method for functionalizing the C–H bonds at the β-position of thiophenes which are often more difficult to activate than those at the α-position.[15] In addition, so far, the preparation of 2′-aryl-2,3′-bithiophene derivatives requires multi-step synthesis and the substrate scope is very limited.[16] Therefore, the potential of Pd-catalyzed 1,4-migration associated with direct arylation for the access to 2-aryl-3-heteroarylthiophenes *via* double C–H bond functionalization needed to be explored. Herein, we report (i) on the regioselectivity of the Pd-catalyzed direct arylations *vs.* Suzuki couplings of 2-(2-bromoaryl)thiophenes and on the scope of the Pd-catalyzed 1,4-migration associated with direct arylation for the formation of 2-aryl-3-heteroarylthiophenes *via* double C–H bond functionalization (Scheme 1c).

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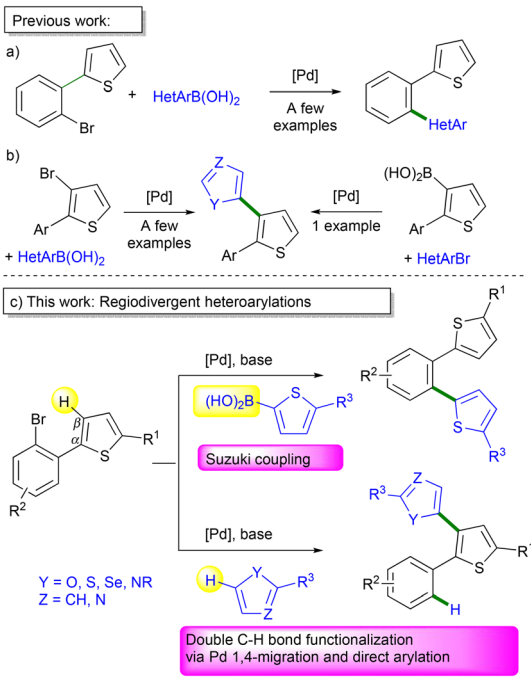
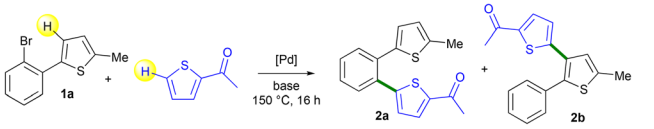


Scheme 1 Pd-catalyzed direct arylation *vs.* Suzuki coupling of 2-(2-bromoaryl)thiophenes and related compounds.

Table 1 Influence of the reaction conditions on the Pd-catalyzed coupling of 2-(2-bromophenyl)-5-methylthiophene **1a** with 2-acetylthiophene[a]



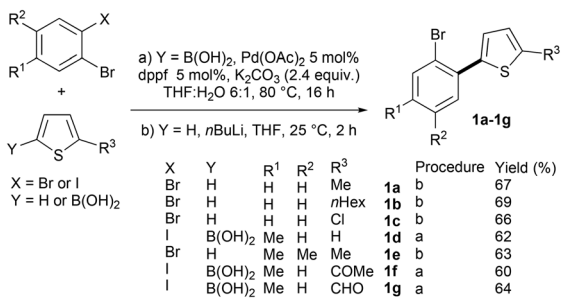
Entry	Catalyst	Solvent	Base	Conv. (%)	Ratio **2a** : **2b**	Yield in **2b** (%)
1	$Pd(OAc)_2$	DMA	KOAc	100	19 : 81	64
2	$Pd(OAc)_2$	DMA	Cs_2CO_3	5	56 : 44	nd
3	$Pd(OAc)_2$	DMA	K_2CO_3	100	46 : 54	nd
4	$Pd(OAc)_2$	DMA	NaOAc	47	19 : 81	nd
5	$Pd(OAc)_2$	DMA	CsOAc	84	40 : 60	nd
6	$Pd(OAc)_2$	DMA	KOPiv	100	33 : 67	nd
7	$PdCl(C_3H_5)(dppb)$	DMA	KOAc	100	24 : 76	61
8	$Pd(OAc)_2$	DMF	KOAc	100	26 : 74	50
9	$Pd(OAc)_2$	NMP	KOAc	100	24 : 76	52
10	$Pd(OAc)_2$	Xylene	KOAc	0	—	0
11	$Pd(OAc)_2$	DEC	KOAc	0	—	0
12	$Pd(OAc)_2$	DMA	KOAc	86	20 : 80	53[b]

[a] [Pd] (0.02 equiv.), 2-acetylthiophene (2 equiv.), 2-(2-bromophenyl)-5-methylthiophene **1a** (1 equiv.), base (3 equiv.), 150 °C, 16 h, **2a** : **2b** ratios, determined by ^{1}H NMR and GC/MS analyses of the crude mixtures, isolated yields. [b] 130 °C.

Results and discussion

First, we prepared a set of 2-(2-bromoaryl)thiophenes *via* Suzuki coupling or base deprotonation (Scheme 2). All the desired products **1a–1g** were obtained in good yields.

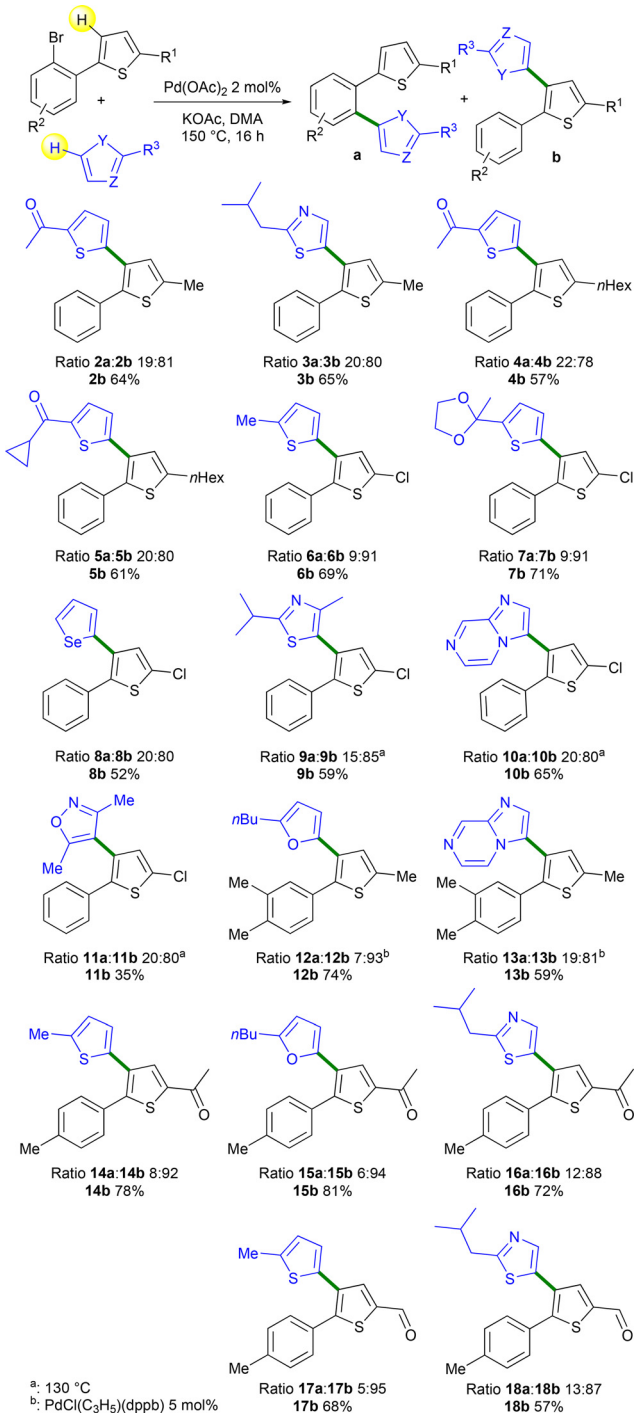
Then, we evaluated the selectivity for the Pd-catalyzed coupling of 2-(2-bromophenyl)-5-methylthiophene **1a** with 2-acetylthiophene (Table 1). The best yield of the desired isomer **2b** arising from the Pd-catalyzed 1,4-migration associated with direct arylation was obtained using 2 mol% $Pd(OAc)_2$ catalyst and the KOAc base in DMA at 150 °C (Table 1, entry 1). Under these conditions, a mixture of **2a** and **2b** was obtained in a 19 : 81 ratio and **2b** was isolated in 64% yield. The use of other bases such as Cs_2CO_3, K_2CO_3, NaOAc, CsOAc or KOPiv led to lower yields of **2b** either due to lower conversions or poor selectivities (Table 1, entries 2–6). In the presence of the $PdCl(C_3H_5)(dppb)$[17] catalyst, a quite similar **2a** : **2b** selectivity and yield of **2b** were obtained (Table 1, entry 7). The influence of a few solvents was also examined but both DMF and NMP led to lower selectivities in **2b**, whereas xylene and diethyl carbonate (DEC) were ineffective (Table 1, entries 8–11). Finally, a lower reaction temperature of 130 °C instead of 150 °C gave **2b** in only 53% yield due to partial conversion of 2-(2-bromophenyl)-5-methylthiophene **1a** (Table 1, entry 12). It should be mentioned that this methodology is limited to the use of 2-(2-bromoaryl)thiophenes, as from 3-(2-bromoaryl)thiophenes, complex mixtures of products were obtained.[18]



	X	Y	R^1	R^2	R^3		Procedure	Yield (%)
	Br	H	H	H	Me	**1a**	b	67
	Br	H	H	H	*n*Hex	**1b**	b	69
	Br	H	H	H	Cl	**1c**	b	66
	I	$B(OH)_2$	Me	H	H	**1d**	a	62
	Br	H	Me	Me	Me	**1e**	b	63
	I	$B(OH)_2$	Me	H	COMe	**1f**	a	60
	I	$B(OH)_2$	Me	H	CHO	**1g**	a	64

Scheme 2 Preparation of 2-(2-bromoaryl)thiophenes **1a–1g**.

Next, the scope of this reaction using several heteroarenes and 2-(2-bromoaryl)thiophenes was investigated (Scheme 3). Using 2-isopropylthiazole and **1a**, a similar **a** : **b** ratio was obtained and product **3b** arising from the Pd 1,4-migration was isolated in 65% yield. 2-(2-Bromophenyl)-5-hexylthiophene **1b** in the presence of 2-acetylthiophene or cyclopropyl-2-thienylketone afforded products **4b** and **5b** in 57% and 61% yields, respectively. No side-reaction on the cyclopropyl unit was detected in the course of this reaction. Then, the β-heteroarylation of the 2-chloro-substituted thiophene derivative **1c** was studied. This reaction is particularly interesting as the access to 4-bromo-2-chlorothiophenes that could provide an alternative synthetic scheme for the preparation of similar products is very challenging.[19] In the presence of 2-methylthiophene or 2-methyl-2-(thiophen-2-yl)-1,3-dioxolane, very high selectivities in favor of the formation of products **b** were observed with the formation of **6b** and **7b** in 69% and 71% yields, respectively. No cleavage of the thienyl C–Cl bond was observed allowing further transformations. In the presence of selenophene, **1c** gave a lower yield of 52% of **8b** due to the for-

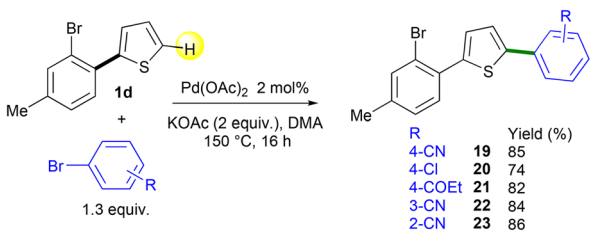


Scheme 3 Heteroarylations of thienyl rings *via* Pd-catalyzed 1,4-migration associated with direct arylation.

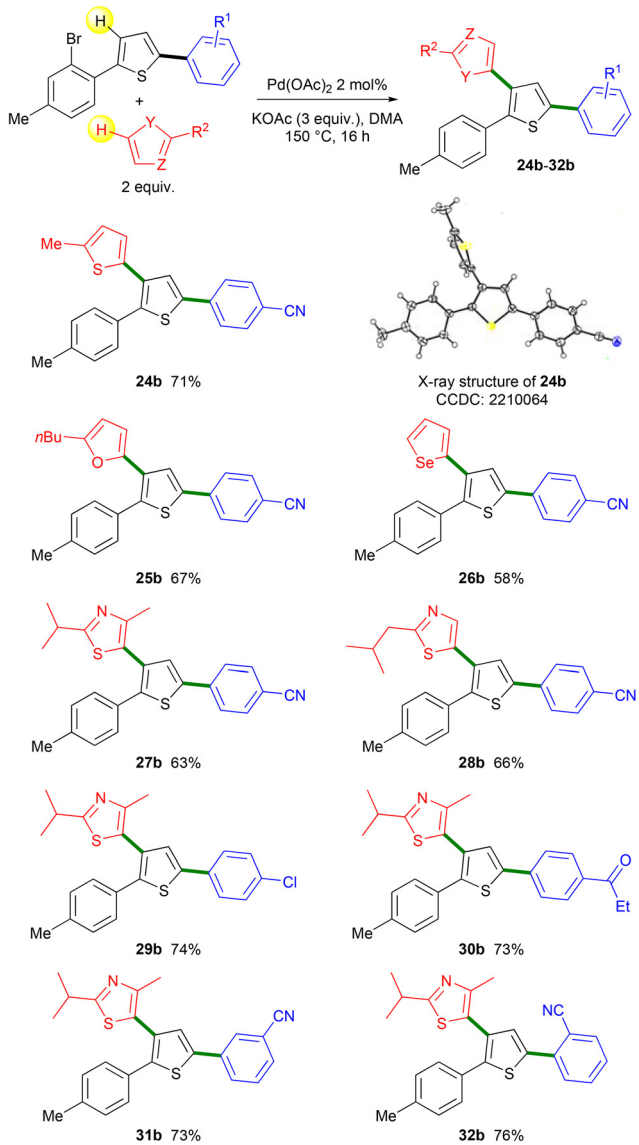
mation of unidentified side-products. 2-Isopropyl-4-methylthiazole, imidazo[1,2-*a*]pyrazine and 3,5-dimethylisoxazole in the presence of **1c** afforded the target Pd 1,4-migration products **9b–11b** in 35–65% yields. These three reactions were performed at a lower temperature of 130 °C due to a partial C–Cl bond cleavage at 150 °C. The reaction also tolerated the presence of two methyl substituents on the benzene ring. However, with this more electron-rich 2-arylthiophene derivative **1e**, 5 mol% $PdCl(C_3H_5)$(dppb) catalyst had to be employed to reach a high conversion. With this catalyst, the target products **12b** and **13b** were obtained in 74% and 59% yields, respectively using 2-butylfuran and imidazo[1,2-*a*]pyrazine as the reaction partners. The reaction also tolerated a 2-acetyl substituent on the thienyl ring. From 2-acetyl-5-arylthiophene **1h** and thiophene, furan and thiazole derivatives as reaction partners, very high selectivities (88–94%) of isomers **b** were observed and the target products **14b–16b** were obtained in 72–81% yields. Finally, the reaction of the 2-formyl-5-arylthiophene derivative **1g** and 2-methylthiophene or 2-isobutylthiazole gave products **17b** and **18b** with 95% and 87% selectivity and in 68% and 57% yields, respectively.

The use of Pd-catalyzed 1,4-migration associated with direct arylation should allow the introduction of an heteroarene regioselectively at one of the two β-positions of the thienyl ring of non-symmetrical 2,5-diarylthiophenes. The heteroarylation should occur at the β-C–H bond on the same side of the thienyl ring bearing the 2-bromoaryl substituent. The starting materials **19–23** were prepared in 74–86% yields by Pd-catalyzed direct C5-arylation from 2-(2-bromoaryl)thiophene **1d** and a set of aryl bromides using the $Pd(OAc)_2$ catalyst with the KOAc base in DMA (Scheme 4). Under these conditions – slight excess (1.3 equiv.) of an electron-poor aryl halide as the reaction partner – no cleavage of the C–Br bond of the bromotoluene unit of **1d** was observed.

Then, the regioselectivity of the direct heteroarylation of 2,5-diarylthiophenes **19–23** was studied (Scheme 5). From 4-(5-(2-bromophenyl)thiophen-2-yl)benzonitrile **19** and 2-methylthiophene, the C4-heteroarylated product **24b** was regioselectively obtained. The regioselectivity of the coupling reaction was determined by X-ray analysis, which confirms that there was no further Pd-migration after the initial Pd 1,4-migration. The reaction also tolerated furan, selenophene and thiazole derivatives as the reaction partners, affording products **25b–28b** in 58–67% yields. From chloro- and propionyl-substituted 2,5-diarylthiophenes **20** and **21**, the expected products **29b** and **30b** were also obtained in high yields. Again, under these conditions, no cleavage of the aryl C–Cl bond was observed allowing further transformations. No significant influence of the position of the nitrile substituent on the benzene ring was observed. Both *meta*- and *ortho*-nitrile-substituted 2,5-diarylthiophenes **22** and **23** led to the desired



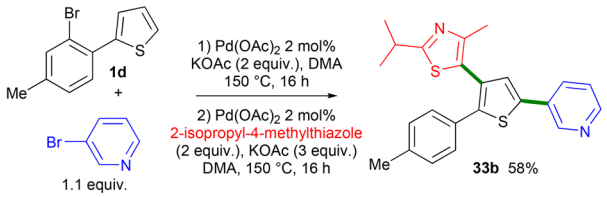
Scheme 4 Pd-catalyzed direct C5-arylation of the thienyl ring of 2-(2-bromoaryl)thiophene **1d**.



Scheme 5 Heteroarylations of thienyl rings *via* Pd-catalyzed 1,4-migration associated with direct arylation.

products **31b** and **32b** in similar yields. It should be mentioned that for all these heteroarylations of 2,5-diarylthiophenes **19–23**, complete regioselectivities in favor of the formation of products **b** arising from Pd 1,4-migration were observed. This selectivity could be due to the conformation of 2,5-diarylthiophenes **19–23** which would favor the Pd 1,4-migration.

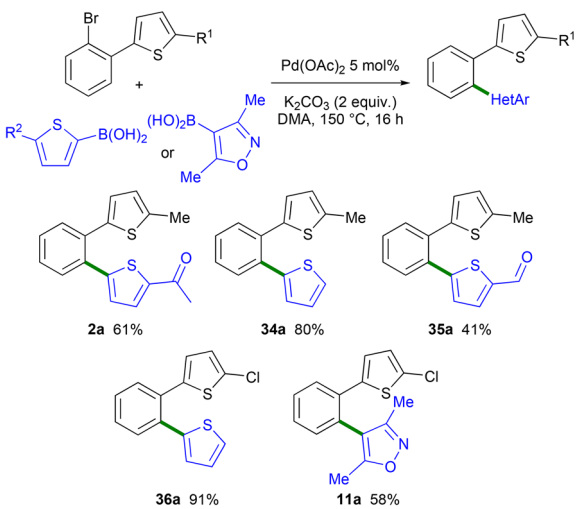
The synthesis of 2,5-diaryl-4-heteroarylthiophene without the isolation of the first arylation compound was also attempted (Scheme 6). From 2-(2-bromo-4-methylphenyl)thiophene **1d**, 3-bromopyridine and 2 mol% $Pd(OAc)_2$ catalyst, the 2,5-diarylated thiophene derivative was obtained in an impure form *via* filtration on a plug of silica. Then, 2-isopropyl-4-methylthiazole, 2 mol% $Pd(OAc)_2$ and KOAc were added to the crude mixture and heated again at 150 °C for 16 h, affording the desired product **33b** in 58% yield.



Scheme 6 Preparation of a tri(hetero)arylated thiophene derivative *via* successive direct heteroarylations.

In order to compare the selectivity of the direct arylation reaction with Suzuki coupling, a few arylations of 2-(2-bromophenyl)-5-methylthiophene **1a** and 2-(2-bromophenyl)-5-chlorothiophene **1c** using arylboronic acids as the reaction partners were performed (Scheme 7). Again using 2 mol% $Pd(OAc)_2$ catalyst and DMA as the solvent, but the K_2CO_3 base instead of a carboxylate base, the formation of the expected 1,2-diheteroaryl-substituted benzene derivatives **2a**, **34a** and **35a** was observed with complete selectivity. It should be mentioned that in the presence of the KOPiv base instead of K_2CO_3, isomer **2a** was obtained with 73% selectivity (27% of **2b**) and in 52% yield indicating that the presence of a carboxylate base favors the Pd 1,4 migration. The reaction of **1c** with 2-thienylboronic acid and the K_2CO_3 base also selectively led to the formation of the expected chloro-substituted 1,2-di(thiophen-2-yl) benzene **36a**. Using **1c** and (3,5-dimethylisoxazol-4-yl)boronic acid as the reaction partner, product **11a** was also obtained with complete selectivity. These results demonstrate that the combination of Pd-catalyzed 1,4 migration reactions associated with direct arylation and Suzuki coupling can be employed as a tool to control regiodivergent heteroarylations.

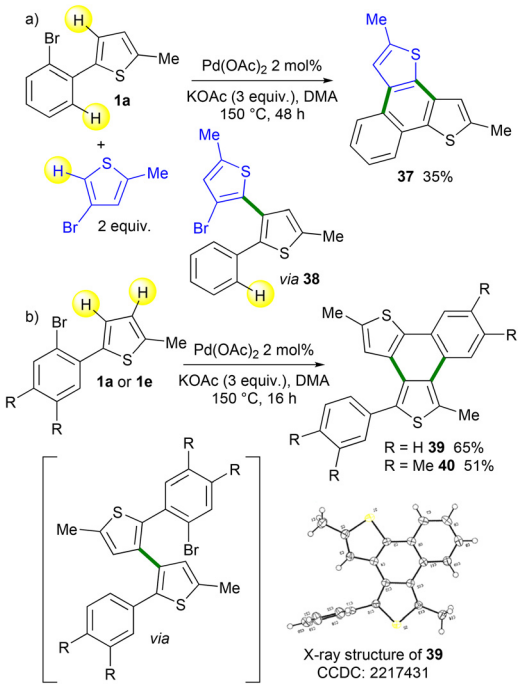
π-Extended polycyclic heteroaromatics[20] have found several applications in the preparation of optoelectronic devices. The topology of the ring fusion and the substituents at their periphery are essential to tune their electronic properties. Therefore, we also attempted to apply the Pd-catalyzed 1,4-



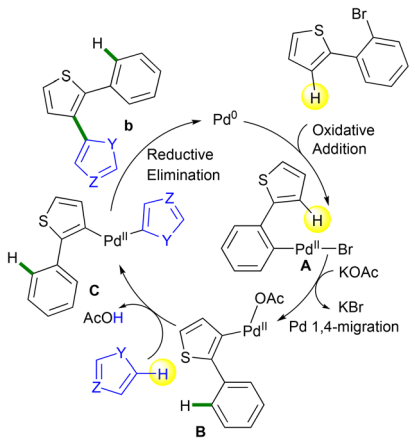
Scheme 7 Heteroarylations of benzene rings *via* Suzuki coupling.

migration associated with direct heteroarylation to the preparation of such products. First, we employed a 4-bromothiophene derivative as a reaction partner with **1a** (Scheme 8a). The desired naphtho[1,2-*b*:3,4-*b*′]dithiophene **37** was obtained in a moderate yield using an extended reaction time (48 h). Intermediate **38** was also isolated in a low yield in an impure form. We also studied the reaction outcome of 2-(2-bromophenyl)-5-methylthiophene **1a** in the absence of the heteroaryl coupling partner (Scheme 8b). The formation of the desired fused polyheteroaromatic naphtho[1,2-*b*:3,4-*c*′]dithiophene **39** in 65% yield was observed. The structure of **39** was confirmed by X-ray analysis. The formation of **39** likely proceeded *via* the initial formation of 2-(2-bromophenyl)-2′-phenyl-3,3′-bithiophene. Then, an intramolecular Pd-catalyzed direct arylation gives naphtho[1,2-*b*:3,4-*c*′]dithiophene **39**. The use of **1e** also provides the corresponding naphtho[1,2-*b*:3,4-*c*′]dithiophene **40** in a moderate yield. This one-pot multi-step synthesis of π-extended polycyclic heteroaromatics is very attractive, as so far very few methods allow the preparation of such fused polyheteroaromatics.[21]

The access to 1,2-bis(heteroaryl)benzenes **a** proceeds certainly *via* a classical Suzuki coupling[22] mechanism, whereas the access to 2′-aryl-2,3′-biheteroarenes **b** occurs likely *via* a Pd 1,4-migration followed by a direct arylation[23] as described in Scheme 9. In both cases, the first step of the catalytic cycle involves the oxidative addition of 2-(2-bromoaryl)thiophene to give intermediate **A**. For Suzuki coupling with arylboronic acids, classical transmetalation followed by reductive elimination gives 1,2-bis(heteroaryl)benzenes **a**. By contrast, with simple heteroarenes using the KOAc base, a Pd 1,4-migration[12]



Scheme 8 Application of the Pd-catalyzed 1,4-migration associated with direct arylation methodology for the preparation of π-extended polycyclic heteroaromatics.



Scheme 9 Proposed catalytic cycle for the access to **b** products.

occurs to give intermediate **B**. Then, after a concerted metallation deprotonation (CMD)[23] of the heteroarene coupling partner, intermediate **C** is obtained. Finally, reductive elimination provides 2′-aryl-2,3′-biheteroarenes **b** with the regeneration of the catalyst.

Conclusions

In summary, the use of either Pd-catalyzed 1,4-migration/direct arylation or Suzuki coupling allowed the regiodivergent heteroarylation of 2-(2-bromoaryl)thiophenes. Using Suzuki coupling, 1,2-diheteroarylbenzenes were obtained. Conversely, the use of C–H heteroarylation conditions led to 2-aryl-3-heteroarylthiophenes due to a Pd 1,4-migration between the aryl and β-position of the thienyl units before heteroarylation. In the course of this coupling reaction, a new C–C bond arises from the functionalization of two C–H bonds. In addition to the advantage of being able to synthesize two classes of products from the same molecular building block, heteroarylation at the β-position of thiophenes by this method is synthetically very attractive because very few β-bromothiophenes, which could allow access to the same products by a classical direct arylation, are commercially available at an affordable cost. The reaction tolerates a variety of heteroarenes and substituents at the C5-position on 2-(2-bromoaryl)thiophenes and provides a new route to π-extended polycyclic heteroaromatics. Moreover, these reactions employ a low loading of air stable palladium sources associated with inexpensive bases. Indeed, we believe that the development of this methodology using other coupling partners for regiodivergent couplings will lead to a powerful tool for organic synthesis.

Experimental

General

DMA (99+%) extra pure and KOAc (99%) were purchased from ACROS and used without purification. All reagents were

weighed and handled in air. All reactions were carried out under an inert atmosphere with standard Schlenk techniques. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer. High-resolution mass spectra were measured on a Bruker MaXis 4G spectrometer. Melting points were determined with a Kofler hot bench system. Chromatography purifications were performed using a CombiFlash NextGen 300 with Buchi FlashPure cartridges containing 40 μm irregular silica.

Preparation of the PdCl(C_3H_5)(dppb) catalyst[17]

An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under an argon atmosphere was charged with [Pd(C_3H_5)Cl]$_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). 10 mL of anhydrous dichloromethane was added, and then the solution was stirred at room temperature for twenty minutes. The solvent was removed under vacuum. The yellow powder was used without purification. ^{31}P NMR (162 MHz, $CDCl_3$) δ = 19.3 (s).

General procedures for the preparation of 2-(2-bromophenyl) thiophenes 1a–1g

Procedure a: As a typical experiment, a mixture of the 1,2-dihalobenzene derivative (3 mmol), the thiophen-2-ylboronic acid derivative (4.5 mmol), 2.0 M K_2CO_3 aq. (3.6 mL), Pd(OAc)$_2$ (33.6 mg, 0.15 mmol) and dppf (83.1 mg, 0.15 mmol) in THF (18 mL) was stirred at 80 °C for 16 h. After being allowed to cool to room temperature, the resulting mixture was extracted with Et_2O (3 × 10 mL). The combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to give 2-(2-bromoaryl)thiophenes.

Procedure b: As a typical experiment, to a solution of the thiophene derivative (12.0 mmol) in THF (25 mL), *n*BuLi was added dropwise (1.55 M in hexane, 7.70 mL, 12.0 mmol) at 0 °C. After being stirred for 1 h, the 1,2-dihalobenzene derivative (10.0 mmol) was added to the solution at the same temperature. Then, the mixture was warmed to room temperature and stirred for 2 h. The residue was purified by column chromatography on silica gel to afford 2-(2-bromoaryl)thiophenes.

2-(2-Bromophenyl)-5-methylthiophene (1a). Following procedure b, from 1,2-dibromobenzene (2.36 g, 10 mmol) and 2-methylthiophene (1.18 g, 12 mmol), **1a** was isolated in 67% (1.69 g) yield as a colorless oil. Eluent pentane.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, J = 8.0, 1.3 Hz, 1H), 7.46 (dd, J = 7.8, 1.7 Hz, 1H), 7.31 (td, J = 7.5, 1.3 Hz, 1H), 7.16 (td, J = 7.5, 1.7 Hz, 1H), 7.11 (d, J = 3.5 Hz, 1H), 6.77 (d, J = 3.5 Hz, 1H), 2.54 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 139.4, 135.7, 133.8, 131.9, 128.8, 127.9, 127.5, 125.4, 122.8, 15.4.

LRMS calcd for $[M]^+$ $C_{11}H_9BrS$ 252, found: 252.

2-(2-Bromophenyl)-5-hexylthiophene (1b). Following procedure b, from 1,2-dibromobenzene (2.36 g, 10 mmol) and 2-hexylthiophene (2.02 g, 12 mmol), **1b** was isolated in 69% (2.23 g) yield as a colorless oil. Eluent pentane.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.32 (t, J = 7.5 Hz, 1H), 7.21–7.12 (m, 2H), 6.81 (d, J = 3.5 Hz, 1H), 2.88 (t, J = 7.4 Hz, 2H), 1.84–1.69 (m, 2H), 1.52–1.29 (m, 6H), 0.95 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.1, 139.1, 135.8, 133.8, 131.8, 128.7, 127.6, 127.4, 124.1, 123.7, 31.7 (m), 30.3, 29.0, 22.7, 14.2.

LRMS calcd for $[M]^+$ $C_{16}H_{19}BrS$ 324, found: 324.

2-(2-Bromophenyl)-5-chlorothiophene (1c). Following procedure b, from 1,2-dibromobenzene (2.36 g, 10 mmol) and 2-chlorothiophene (1.42 g, 12 mmol), **1c** was isolated in 66% (1.80 g) yield as a yellow oil. Eluent pentane.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, J = 8.0, 1.3 Hz, 1H), 7.43 (dd, J = 7.8, 1.7 Hz, 1H), 7.33 (td, J = 7.6, 1.3 Hz, 1H), 7.19 (td, J = 7.7, 1.7 Hz, 1H), 7.06 (d, J = 3.8 Hz, 1H), 6.93 (d, J = 3.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 134.6, 133.9, 131.8, 130.7, 129.5, 127.7, 127.2, 126.2, 122.8.

LRMS calcd for $[M]^+$ $C_{10}H_6BrClS$ 274, found: 274.

2-(2-Bromo-4-methylphenyl)thiophene (1d). Following procedure a, from 2-bromo-1-iodo-4-methylbenzene (0.891 g, 3 mmol) and 2-thienylboronic acid (0.576 g, 4.5 mmol), **1d** was isolated in 62% (0.471 g) yield as a colorless oil. Eluent pentane.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (s, 1H), 7.39–7.34 (m, 2H), 7.27 (dd, J = 5.6, 1.2 Hz, 1H), 7.13 (d, J = 7.7 Hz, 1H), 7.10 (dd, J = 5.2, 3.6 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 139.5, 134.2, 132.5, 131.8, 128.4, 127.6, 127.0, 125.9, 122.7, 20.9.

LRMS calcd for $[M]^+$ $C_{11}H_9BrS$ 252, found: 252.

2-(2-Bromo-4,5-dimethylphenyl)-5-methylthiophene (1e). Following procedure b, from 1,2-dibromo-4,5-dimethylbenzene (2.64 g, 10 mmol) and 2-methylthiophene (1.18 g, 12 mmol), **1e** was isolated in 63% (1.77 g) yield as a colorless oil. Eluent pentane.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H), 7.27 (s, 1H), 7.11 (d, J = 3.5 Hz, 1H), 6.79 (d, J = 3.5 Hz, 1H), 2.57 (s, 3H), 2.29 (s, 3H), 2.26 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.3, 139.6, 137.8, 136.1, 134.4, 132.8, 132.7, 127.4, 125.3, 119.2, 19.3, 19.2, 15.4.

LRMS calcd for $[M]^+$ $C_{13}H_{13}BrS$ 280, found: 280.

1-(5-(2-Bromo-4-methylphenyl)thiophen-2-yl)ethan-1-one (1f). Following procedure a, from 2-bromo-1-iodo-4-methylbenzene (0.891 g, 3 mmol) and 5-acetyl-2-thienylboronic acid (0.765 g, 4.5 mmol), **1f** was isolated in 60% (0.531 g) yield as a yellow oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 3.5 Hz, 1H), 7.51 (s, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 3.5 Hz, 1H), 7.15 (d, J = 7.8 Hz, 1H), 2.57 (s, 3H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 150.4, 144.2, 140.7, 134.5, 132.3, 131.5, 131.4, 128.7, 128.6, 122.3, 26.8, 20.9.

LRMS calcd for $[M]^+$ $C_{13}H_{11}BrOS$ 296, found: 296.

5-(2-Bromo-4-methylphenyl)thiophene-2-carbaldehyde (1g). Following procedure a, from 2-bromo-1-iodo-4-methylbenzene (0.891 g, 3 mmol) and 5-formyl-2-thienylboronic acid (0.702 g, 4.5 mmol), **1g** was isolated in 64% (0.539 g) yield as a colorless oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.91 (s, 1H), 7.73 (d, J = 3.5 Hz, 1H), 7.52 (s, 1H), 7.39–7.34 (m, 2H), 7.16 (d, J = 7.8 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 183.0, 151.9, 143.6, 141.0, 136.2, 134.5, 131.5, 131.2, 128.8, 128.7, 122.3, 20.9.

LRMS calcd for $[M]^+$ $C_{12}H_9BrOS$ 280, found: 280.

General procedure for the preparation of 2′-aryl-2,3′-biheteroarenes 2b–18b

As a typical experiment, the reaction of the 2-(2-bromoaryl) thiophene derivatives **1a–1g** (1 mmol), heteroarene (2 mmol) and KOAc (0.294 g, 3 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon afforded the coupling product after evaporation of the solvent and purification on silica gel. The **a : b** ratios were determined by ^{1}H NMR and GC/MS analyses of the crude mixtures.

1-(5′-Methyl-2′-phenyl-[2,3′-bithiophen]-5-yl)ethan-1-one (2b). From 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol) and 2-acetylthiophene (0.252 g, 2 mmol), a mixture of **2a** and **2b** was obtained in a 19 : 81 ratio and **2b** was isolated in 64% (0.191 g) yield as a white solid: mp 92–94 °C. Eluent pentane, R_f **2a** = 0.30, R_f **2b** = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 3.9 Hz, 1H), 7.40–7.32 (m, 5H), 6.91 (s, 1H), 6.79 (d, J = 3.9 Hz, 1H), 2.51 (s, 3H), 2.49 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 147.5, 142.6, 139.4, 138.7, 133.8, 133.0, 129.8, 129.7, 128.8, 128.4, 127.5, 126.5, 26.7, 15.3.

HRMS calcd for $[M + H]^+$ $C_{17}H_{15}OS_2$ 299.0559, found: 299.0557.

2-Isobutyl-5-(5-methyl-2-phenylthiophen-3-yl)thiazole (3b). From 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol) and 2-isobutylthiazole (0.282 g, 2 mmol), a mixture of **3a** and **3b** was obtained in a 20 : 80 ratio and **3b** was isolated in 65% (0.203 g) yield as a colorless oil. Eluent pentane, R_f **3a** = 0.20, R_f **3b** = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 1H), 7.39–7.30 (m, 5H), 6.86 (s, 1H), 2.77 (d, J = 7.6 Hz, 2H), 2.50 (s, 3H), 2.09–1.99 (m, 1H), 0.95 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 139.9, 139.1, 137.5, 133.9, 132.5, 129.9, 128.7, 128.2, 127.6, 127.5, 42.4, 29.8, 22.4, 15.3.

HRMS calcd for $[M + H]^+$ $C_{18}H_{20}NS_2$ 314.1032, found: 314.1029.

1-(5′-Hexyl-2′-phenyl-[2,3′-bithiophen]-5-yl)ethan-1-one (4b). From 2-(2-bromophenyl)-5-hexylthiophene **1b** (0.323 g, 1 mmol) and 2-acetylthiophene (0.252 g, 2 mmol), a mixture of **4a** and **4b** was obtained in a 22 : 78 ratio and **4b** was isolated in 57% (0.210 g) yield as a yellow oil. Eluent pentane, R_f **4a** = 0.27, R_f **4b** = 0.30.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (d, J = 4.0 Hz, 1H), 7.41–7.32 (m, 5H), 6.92 (s, 1H), 6.80 (d, J = 4.0 Hz, 1H), 2.81 (t, J = 7.6 Hz, 2H), 2.49 (s, 3H), 1.72 (quint., J = 7.6 Hz, 2H), 1.49–1.39 (m, 2H), 1.39–1.30 (m, 4H), 0.91 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 147.6, 145.6, 142.5, 138.4, 133.9, 133.0, 129.8, 129.5, 128.8, 128.3, 126.5, 126.3, 31.7, 31.5, 30.1, 28.9, 26.7, 22.7, 14.2.

HRMS calcd for $[M + H]^+$ $C_{22}H_{25}OS_2$ 369.1341, found: 369.1341.

Cyclopropyl(5′-hexyl-2′-phenyl-[2,3′-bithiophen]-5-yl)methanone (5b). From 2-(2-bromophenyl)-5-hexylthiophene **1b** (0.323 g, 1 mmol) and cyclopropyl(thiophen-2-yl)methanone (0.304 g, 2 mmol), a mixture of **5a** and **5b** was obtained in a 20 : 80 ratio and **5b** was isolated in 61% (0.240 g) yield as a yellow oil. Eluent pentane/EtOAc 80/20, R_f **5a** = 0.29, R_f **5b** = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 4.0 Hz, 1H), 7.42–7.32 (m, 5H), 6.93 (s, 1H), 6.83 (d, J = 4.0 Hz, 1H), 2.81 (t, J = 7.6 Hz, 2H), 2.50–2.39 (m, 1H), 1.72 (quint., J = 7.6 Hz, 2H), 1.49–1.38 (m, 2H), 1.38–1.28 (m, 4H), 1.25–1.18 (m, 2H), 1.02–0.95 (m, 2H), 0.91 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 192.8, 147.0, 145.5, 143.0, 138.3, 134.0, 131.9, 129.8, 129.6, 128.8, 128.3, 126.6, 126.4, 31.7, 31.6, 30.1, 29.0, 22.7, 17.9, 14.2, 11.3.

HRMS calcd for $[M + H]^+$ $C_{24}H_{27}OS_2$ 395.1498, found: 395.1503.

5′-Chloro-5-methyl-2′-phenyl-2,3′-bithiophene (6b). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.273 g, 1 mmol) and 2-methylthiophene (0.196 g, 2 mmol), a mixture of **6a** and **6b** was obtained in a 9 : 91 ratio and **6b** was isolated in 69% (0.201 g) yield as a colorless oil. Eluent pentane, R_f **6a** = 0.30, R_f **6b** = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.31 (m, 5H), 7.01 (s, 1H), 6.66 (d, J = 3.5 Hz, 1H), 6.55 (d, J = 3.5 Hz, 1H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.9, 136.2, 135.0, 133.3, 130.8, 130.0, 128.8, 128.7, 128.5, 128.4, 126.1, 125.5, 15.4.

HRMS calcd for $[M + H]^+$ $C_{15}H_{12}ClS_2$ 291.0064, found: 291.0064.

2-(5′-Chloro-2′-phenyl-[2,3′-bithiophen]-5-yl)-2-methyl-1,3-dioxolane (7b). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.273 g, 1 mmol) and 2-methyl-2-(thiophen-2-yl)-1,3-dioxolane (0.340 g, 2 mmol), a mixture of **7a** and **7b** was obtained in a 9 : 91 ratio and **7b** was isolated in 71% (0.257 g) yield as a yellow solid: mp 128–130 °C. Eluent pentane/EtOAc 80/20, R_f **7a** = 0.23, R_f **7b** = 0.27.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.31 (m, 5H), 7.02 (s, 1H), 6.82 (d, J = 3.7 Hz, 1H), 6.67 (d, J = 3.7 Hz, 1H), 4.05–3.98 (m, 2H), 3.98–3.91 (m, 2H), 1.74 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 147.0, 137.0, 136.9, 133.1, 130.3, 129.9, 129.0, 128.8, 128.6, 128.4, 125.9, 124.4, 107.2, 65.1, 27.5.

HRMS calcd for $[M + H]^+$ $C_{18}H_{16}ClO_2S_2$ 363.0275, found: 363.0277.

5-Chloro-2-phenyl-3-(selenophen-2-yl)thiophene (8b). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.273 g, 1 mmol) and selenophene (0.262 g, 2 mmol), a mixture of **8a** and **8b** was obtained in a 20 : 80 ratio and **11b** was isolated in 52% (0.168 g) yield as a colorless oil. Eluent pentane, R_f **8a** = 0.29, R_f **8b** = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, J = 5.6, 1.2 Hz, 1H), 7.43–7.36 (m, 5H), 7.15 (dd, J = 5.6, 3.8 Hz, 1H), 7.11 (dd, J = 3.8, 1.2 Hz, 1H), 7.06 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.7, 136.6, 133.0, 132.8, 131.0, 130.3, 129.6, 128.9, 128.8, 128.5, 128.3.

HRMS calcd for $[M + H]^+$ $C_{14}H_{10}ClSSe$ 324.9351, found: 324.9350.

5-(5-Chloro-2-phenylthiophen-3-yl)-2-isopropyl-4-methylthiazole (9b). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.273 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), a mixture of **9a** and **9b** was obtained in a 15 : 85 ratio and **9b** was isolated in 59% (0.197 g) yield as a yellow solid: mp 91–93 °C. Eluent pentane/EtOAc 80/20, R_f **9a** = 0.26, R_f **9b** = 0.30.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31–7.15 (m, 5H), 6.89 (s, 1H), 3.23 (sept., J = 7.6 Hz, 1H), 2.01 (s, 3H), 1.37 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.8, 149.0, 140.2, 133.2, 130.1, 128.9, 128.8, 128.5, 128.2, 127.3, 123.8, 33.5, 23.3, 15.8.

HRMS calcd for $[M + H]^+$ $C_{17}H_{17}ClNS_2$ 334.0486, found: 334.0489.

3-(5-Chloro-2-phenylthiophen-3-yl)imidazo[1,2-*a*]pyrazine (10b). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.273 g, 1 mmol) and imidazo[1,2-*a*]pyrazine (0.238 g, 2 mmol), a mixture of **10a** and **10b** was obtained in a 20 : 80 ratio and **10b** was isolated in 65% (0.203 g) yield as a white solid: mp 140–142 °C. Eluent pentane/EtOAc 60/40, R_f **10a** = 0.21, R_f **10b** = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.08 (d, J = 1.5 Hz, 1H), 7.78 (s, 1H), 7.64 (d, J = 4.6 Hz, 1H), 7.49 (dd, J = 4.6, 1.5 Hz, 1H), 7.27–7.17 (m, 3H), 7.09 (d, J = 8.2 Hz, 2H), 7.03 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 141.0, 140.9, 135.7, 132.6, 130.6, 129.7, 129.4, 129.0, 128.9, 127.5, 122.6, 121.2, 116.9.

HRMS calcd for $[M + H]^+$ $C_{16}H_{11}ClN_3S$ 312.0357, found: 312.0354.

4-(5-Chloro-2-phenylthiophen-3-yl)-3,5-dimethylisoxazole (11b). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.273 g, 1 mmol) and 3,5-dimethylisoxazole (0.194 g, 2 mmol), a mixture of **11a** and **11b** was obtained in a 20 : 80 ratio and **11b** was isolated in 35% (0.101 g) yield as a white solid: mp 86–88 °C. Eluent pentane/EtOAc 80/20, R_f **11a** = 0.30, R_f **11b** = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.27 (m, 3H), 7.23–7.19 (m, 2H), 6.79 (s, 1H), 2.06 (s, 3H), 1.98 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 159.2, 140.1, 133.2, 129.2, 129.1, 129.0, 128.2, 128.0, 125.0, 111.2, 11.4, 10.5.

HRMS calcd for $[M + H]^+$ $C_{15}H_{13}ClNOS$ 290.0401, found: 290.0402.

2-Butyl-5-(2-(3,4-dimethylphenyl)-5-methylthiophen-3-yl)furan (12b). From 2-(2-bromo-4,5-dimethylphenyl)-5-methylthiophene **1e** (0.281 g, 1 mmol) and 2-butylfuran (0.248 g, 2 mmol), a mixture of **12a** and **12b** was obtained in a 7 : 93 ratio and **12b** was isolated in 74% (0.240 g) yield as a yellow oil. Eluent pentane, R_f **12a** = 0.14, R_f **12b** = 0.17.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (s, 1H), 7.19 (d, J = 7.7 Hz, 1H), 7.11 (d, J = 7.7 Hz, 1H), 6.99 (q, J = 1.1 Hz, 1H), 6.01 (d, J = 3.2 Hz, 1H), 5.88 (d, J = 3.2 Hz, 1H), 2.57 (t, J = 7.6 Hz, 2H), 2.49 (d, J = 1.1 Hz, 3H), 2.29 (s, 3H), 2.27 (s, 3H), 1.57 (quint., J = 7.6 Hz, 2H), 1.35 (sext., J = 7.6 Hz, 2H), 0.91 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 149.0, 138.3, 136.5, 136.2, 135.1, 132.3, 130.8, 129.7, 127.6, 127.1, 125.6, 107.0, 106.3, 30.4, 27.9, 22.4, 19.9, 19.7, 15.3, 14.0.

HRMS calcd for $[M + H]^+$ $C_{21}H_{25}OS$ 325.1621, found: 325.1625.

3-(2-(3,4-Dimethylphenyl)-5-methylthiophen-3-yl)imidazo[1,2-*a*]pyrazine (13b). From 2-(2-bromo-4,5-dimethylphenyl)-5-methylthiophene **1e** (0.281 g, 1 mmol) and imidazo[1,2-*a*]pyrazine (0.238 g, 2 mmol), a mixture of **13a** and **13b** was obtained in a 19 : 81 ratio and **13b** was isolated in 59% (0.188 g) yield as a colorless oil. Eluent pentane/EtOAc 60/40, R_f **13a** = 0.20, R_f **13b** = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.08 (s, 1H), 7.78 (s, 1H), 7.63 (d, J = 4.6 Hz, 1H), 7.46–7.43 (m, 2H), 7.21 (s, 1H), 6.41–6.35 (m, 2H), 2.38 (s, 3H), 2.33 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 140.9, 140.8, 139.1, 139.0, 136.7, 135.6, 133.6, 132.6, 131.4, 129.3, 126.5, 125.8, 125.5, 123.3, 116.9, 19.8, 19.5, 15.3.

HRMS calcd for $[M + H]^+$ $C_{19}H_{18}N_3S$ 320.1216, found: 320.1214.

1-(5-Methyl-2′-(*p*-tolyl)-[2,3′-bithiophen]-5′-yl)ethan-1-one (14b). From 1-(5-(2-bromo-4-methylphenyl)thiophen-2-yl)ethan-1-one **1f** (0.295 g, 1 mmol) and 2-methylthiophene (0.196 g, 2 mmol), a mixture of **14a** and **14b** was obtained in an 8 : 92 ratio and **14b** was isolated in 78% (0.243 g) yield as a yellow oil. Eluent pentane/EtOAc 80/20, R_f **14a** = 0.14, R_f **14b** = 0.17.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 6.71 (d, J = 3.5 Hz, 1H), 6.59 (d, J = 3.5 Hz, 1H), 2.57 (s, 3H), 2.73 (s, 3H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.6, 146.8, 141.7, 140.1, 139.1, 134.8, 134.6, 132.2, 130.3, 129.5, 129.4, 126.3, 125.5, 26.6, 21.4, 15.3.

HRMS calcd for $[M + H]^+$ $C_{18}H_{17}OS_2$ 313.0715, found: 313.0715.

1-(4-(5-Butylfuran-2-yl)-5-(*p*-tolyl)thiophen-2-yl)ethan-1-one (15b). From 1-(5-(2-bromo-4-methylphenyl)thiophen-2-yl) ethan-1-one **1f** (0.295 g, 1 mmol) and 2-butylfuran (0.248 g, 2 mmol), a mixture of **15a** and **15b** was obtained in a 6 : 94 ratio and **15b** was isolated in 81% (0.274 g) yield as a yellow oil. Eluent pentane/EtOAc 80/20, R_f **15a** = 0.33, R_f **15b** = 0.37.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 6.03 (d, J = 3.5 Hz, 1H), 5.91 (d, J = 3.5 Hz, 1H), 2.64–2.55 (m, 5H), 2.40 (s, 3H), 1.58 (quint., J = 7.6 Hz, 2H), 1.35 (sext., J = 7.6 Hz, 2H), 0.92 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 155.9, 147.4, 145.4, 142.3, 139.1, 132.3, 130.7, 129.5, 129.4, 129.3, 108.2, 106.6, 30.3, 27.8, 26.7, 22.4, 21.5, 13.9.

LRMS calcd for $[M]^+$ $C_{21}H_{22}O_2S$ 338, found: 338.

HRMS calcd for $[M + H]^+$ $C_{21}H_{23}O_2S$ 339.1413, found: 339.1414.

1-(4-(2-Isobutylthiazol-5-yl)-5-(*p*-tolyl)thiophen-2-yl)ethan-1-one (16b). From 1-(5-(2-bromo-4-methylphenyl)thiophen-2-yl) ethan-1-one **1f** (0.295 g, 1 mmol) and 2-isobutylthiazole

(0.282 g, 2 mmol), a mixture of **16a** and **16b** was obtained in a 12 : 88 ratio and **16b** was isolated in 58% (0.256 g) yield as a yellow solid: mp 87–89 °C. Eluent pentane/EtOAc 80/20, R_f **16a** = 0.20, R_f **16b** = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (s, 1H), 7.51 (s, 1H), 7.27 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 2.80 (d, J = 7.6 Hz, 2H), 2.57 (s, 3H), 2.38 (s, 3H), 2.10–2.02 (m, 1H), 0.96 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5, 170.4, 148.4, 142.3, 140.6, 139.6, 134.2, 131.1, 129.7, 129.6, 129.4, 128.7, 42.4, 29.8, 26.7, 22.3, 21.5.

HRMS calcd for $[M + H]^+$ $C_{20}H_{22}NOS_2$ 356.1137, found: 356.1136.

5-Methyl-2′-(*p*-tolyl)-[2,3′-bithiophene]-5′-carbaldehyde (17b). From 5-(2-bromo-4-methylphenyl)thiophene-2-carbaldehyde **1g** (0.281 g, 1 mmol) and 2-methylthiophene (0.196 g, 2 mmol), a mixture of **17a** and **17b** was obtained in a 5 : 95 ratio and **17b** was isolated in 68% (0.203 g) yield as a yellow oil. Eluent pentane/EtOAc 80/20, R_f **17a** = 0.23, R_f **17b** = 0.27.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.88 (s, 1H), 7.79 (s, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 6.72 (d, J = 3.5 Hz, 1H), 6.60 (d, J = 3.5 Hz, 1H), 2.44 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 182.9, 148.2, 141.2, 140.4, 139.5, 138.4, 134.4, 132.6, 130.2, 129.6, 129.4, 126.5, 125.6, 21.5, 15.4.

HRMS calcd for $[M + H]^+$ $C_{17}H_{15}OS_2$ 299.0559, found: 299.0557.

4-(2-Isobutylthiazol-5-yl)-5-(*p*-tolyl)thiophene-2-carbaldehyde (18b). From 5-(2-bromo-4-methylphenyl)thiophene-2-carbaldehyde **1g** (0.281 g, 1 mmol) and 2-isobutylthiazole (0.282 g, 2 mmol), a mixture of **18a** and **18b** was obtained in a 13 : 87 ratio and **18b** was isolated in 57% (0.194 g) yield as a yellow solid: mp 90–92 °C. Eluent pentane/EtOAc 80/20, R_f **18a** = 0.10, R_f **18b** = 0.12.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.80 (s, 1H), 7.53 (s, 1H), 7.28 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 2.80 (d, J = 7.6 Hz, 2H), 2.39 (s, 3H), 2.10–2.02 (m, 1H), 0.97 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 182.7, 170.6, 149.8, 141.6, 140.8, 140.0, 138.0, 130.8, 129.7, 129.5, 129.4, 129.1, 42.4, 29.8, 22.3, 21.5.

HRMS calcd for $[M + H]^+$ $C_{19}H_{20}NOS_2$ 342.0981, found: 342.0981.

General procedure for the preparation of 2,5-diarylthiophenes 19–23

As a typical experiment, the reaction of 2-(2-bromo-4-methylphenyl)thiophene **1d** (0.253 g, 1 mmol), aryl bromide (1.3 mmol) and KOAc (0.196 g, 2 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the coupling product after evaporation of the solvent and purification on silica gel.

4-(5-(2-Bromophenyl)thiophen-2-yl)benzonitrile (19). From 2-(2-bromo-4-methylphenyl)thiophene **1d** (0.253 g, 1 mmol) and 4-bromobenzonitrile (0.237 g, 1.3 mmol), **19** was isolated in 85% (0.301 g) yield as a yellow oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.52 (s, 1H), 7.40–7.36 (m, 2H), 7.28 (d, J = 3.7 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 2.36 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.6, 142.1, 140.0, 138.5, 134.4, 132.8, 131.6, 131.4, 129.0, 128.5, 125.9, 125.1, 122.3, 118.9, 110.6, 20.8.

LRMS calcd for $[M]^+$ $C_{18}H_{12}BrNS$ 353, found: 353.

2-(2-Bromo-4-methylphenyl)-5-(4-chlorophenyl)thiophene (20). From 2-(2-bromo-4-methylphenyl)thiophene **1d** (0.253 g, 1 mmol) and 1-bromo-4-chlorobenzene (0.249 g, 1.3 mmol), **20** was isolated in 74% (0.269 g) yield as a yellow oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 8.3 Hz, 2H), 7.53 (s, 1H), 7.40 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 8.3 Hz, 2H), 7.29–7.23 (m, 2H), 7.15 (d, J = 8.1 Hz, 1H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.4, 141.7, 139.6, 134.3, 133.4, 132.9, 132.1, 131.5, 129.2, 128.7, 128.5, 127.0, 123.4, 122.4, 20.8.

LRMS calcd for $[M]^+$ $C_{17}H_{12}BrClS$ 364, found: 364.

1-(4-(5-(2-Bromo-4-methylphenyl)thiophen-2-yl)phenyl)propan-1-one (21). From 2-(2-bromo-4-methylphenyl)thiophene **1d** (0.253 g, 1 mmol) and 4-bromopropiophenone (0.277 g, 1.3 mmol), **21** was isolated in 82% (0.316 g) yield as a colorless oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 8.3 Hz, 2H), 7.52 (s, 1H), 7.43–7.38 (m, 2H), 7.28 (d, J = 3.7 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 3.00 (q, J = 7.6 Hz, 2H), 2.37 (s, 3H), 1.25 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.1, 143.3, 143.0, 139.9, 138.6, 135.7, 134.4, 132.0, 131.5, 129.0, 128.9, 128.5, 125.6, 124.5, 122.4, 31.9, 20.9, 8.4.

LRMS calcd for $[M]^+$ $C_{20}H_{17}BrOS$ 384, found: 384.

3-(5-(2-Bromo-4-methylphenyl)thiophen-2-yl)benzonitrile (22). From 2-(2-bromo-4-methylphenyl)thiophene **1d** (0.253 g, 1 mmol) and 3-bromobenzonitrile (0.237 g, 1.3 mmol), **22** was isolated in 84% (0.297 g) yield as a yellow oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (s, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.57–7.51 (m, 2H), 7.48 (t, J = 7.8 Hz, 1H), 7.39 (d, J = 8.3 Hz, 1H), 7.33 (d, J = 3.7 Hz, 1H), 7.27 (d, J = 3.7 Hz, 1H), 7.16 (d, J = 8.1 Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 141.8, 140.0, 135.7, 134.4, 131.8, 131.5, 130.7, 129.9, 129.8, 129.1, 128.9, 128.5, 124.4, 122.4, 118.7, 113.3, 20.9.

LRMS calcd for $[M]^+$ $C_{18}H_{12}BrNS$ 353, found: 353.

2-(5-(2-Bromo-4-methylphenyl)thiophen-2-yl)benzonitrile (23). From 2-(2-bromo-4-methylphenyl)thiophene **1d** (0.253 g, 1 mmol) and 2-bromobenzonitrile (0.237 g, 1.3 mmol), **23** was isolated in 86% (0.304 g) yield as a yellow oil. Eluent pentane/EtOAc 95/5.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.3 Hz, 1H), 7.68–7.63 (m, 2H), 7.59 (t, J = 7.8 Hz, 1H), 7.52 (s, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.37 (t, J = 7.8 Hz, 1H), 7.31 (d, J = 3.7 Hz, 1H), 7.15 (d, J = 8.1 Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 139.9, 139.7, 137.4, 134.5, 134.4, 133.1, 131.7, 131.6, 129.5, 128.7, 128.5, 127.6, 127.5, 122.3, 119.0, 109.8, 20.8.

LRMS calcd for $[M]^+$ $C_{18}H_{12}BrNS$ 353, found: 353.

General procedure for the preparation of heteroarylated 2,3-diarylthiophenes 24b–32b

As a typical experiment, the reaction of the 2-(2-bromophenyl)-5-arylthiophene derivative **19–23** (1 mmol), heteroarene (2 mmol) and KOAc (0.294 g, 3 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the coupling product after evaporation of the solvent and purification on silica gel.

4-(5-Methyl-2′-(*p*-tolyl)-[2,3′-bithiophen]-5′-yl)benzonitrile (24b). From 4-(5-(2-bromophenyl)thiophen-2-yl)benzonitrile **19** (0.340 g, 1 mmol) and 2-methylthiophene (0.196 g, 2 mmol), **24b** was isolated in 71% (0.263 g) yield as a yellow solid: mp 144–146 °C. Eluent pentane/EtOAc 80/20, R_f = 0.30.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.45 (s, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 6.74 (d, J = 3.5 Hz, 1H), 6.60 (d, J = 3.5 Hz, 1H), 2.45 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 139.9, 139.8, 139.7, 138.6, 138.4, 135.4, 132.9, 132.5, 130.6, 129.6, 129.5, 127.6, 126.1, 125.8, 125.6, 119.0, 110.8, 21.5, 15.4.

>HRMS calcd for $[M + H]^+$ $C_{23}H_{18}NS_2$ 372.0875, found: 372.0874.

4-(4-(5-Butylfuran-2-yl)-5-(*p*-tolyl)thiophen-2-yl)benzonitrile (25b). From 4-(5-(2-bromophenyl)thiophen-2-yl)benzonitrile **19** (0.340 g, 1 mmol) and 2-butylfuran (0.248 g, 2 mmol), **25b** was isolated in 67% (0.266 g) yield as a yellow solid: mp 82–84 °C. Eluent pentane/EtOAc 80/20, R_f = 0.27.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 7.63 (s, 1H), 7.40 (d, J = 8.1 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 6.08 (d, J = 3.2 Hz, 1H), 5.93 (d, J = 3.2 Hz, 1H), 2.62 (t, J = 7.6 Hz, 2H), 2.42 (s, 3H), 1.59 (quint., J = 7.6 Hz, 2H), 1.37 (sext., J = 7.6 Hz, 2H), 0.94 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 148.0, 140.0, 138.7, 138.5, 138.4, 132.8, 131.0, 129.6, 129.4, 129.3, 125.8, 125.3, 119.0, 110.7, 107.9, 106.6, 30.3, 27.9, 22.4, 21.4, 13.9.

HRMS calcd for $[M + H]^+$ $C_{26}H_{24}NOS$ 398.1573, found: 398.1574.

4-(4-(Selenophen-2-yl)-5-(*p*-tolyl)thiophen-2-yl)benzonitrile (26b). From 4-(5-(2-bromophenyl)thiophen-2-yl)benzonitrile **19** (0.340 g, 1 mmol) and selenophene (0.262 g, 2 mmol), **26b** was isolated in 58% (0.235 g) yield as a white solid: mp 162–164 °C. Eluent pentane/EtOAc 80/20, R_f = 0.27.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (dd, J = 4.8, 1.8 Hz, 1H), 7.71 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H), 7.50 (s, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.22–7.16 (m, 4H), 2.40 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.3, 140.3, 139.7, 138.9, 138.3, 134.5, 132.9, 130.9, 130.3, 129.9, 129.7, 129.6, 128.5, 127.6, 125.9, 118.9, 110.9, 21.5.

HRMS calcd for $[M + H]^+$ $C_{22}H_{16}NSSe$ 406.0163, found: 406.0164.

4-(4-(2-Isopropyl-4-methylthiazol-5-yl)-5-(*p*-tolyl)thiophen-2-yl) benzonitrile (27b). From 4-(5-(2-bromophenyl)thiophen-2-yl) benzonitrile **19** (0.340 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), **27b** was isolated in 63% (0.261 g) yield as a white solid: mp 144–146 °C. Eluent pentane/EtOAc 80/20, R_f = 0.17.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.35 (s, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 3.26 (sept., J = 7.6 Hz, 1H), 2.35 (s, 3H), 2.04 (s, 3H), 1.40 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 148.9, 143.4, 139.6, 138.4, 138.2, 132.9, 130.6, 129.7, 129.3, 128.9, 128.2, 125.8, 124.2, 118.9, 110.9, 33.5, 23.3, 21.4, 15.9.

HRMS calcd for $[M + H]^+$ $C_{25}H_{23}N_2S_2$ 415.1297, found: 415.1296.

4-(4-(2-Isobutylthiazol-5-yl)-5-(*p*-tolyl)thiophen-2-yl)benzonitrile (28b). From 4-(5-(2-bromophenyl)thiophen-2-yl)benzonitrile **19** (0.340 g, 1 mmol) and 2-isobutylthiazole (0.282 g, 2 mmol), **28b** was isolated in 66% (0.274 g) yield as a yellow solid: mp 140–142 °C. Eluent pentane/EtOAc 80/20, R_f = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H), 7.55 (s, 1H), 7.47 (s, 1H), 7.30 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 2.80 (d, J = 7.6 Hz, 2H), 2.40 (s, 3H), 2.11–2.03 (m, 1H), 0.97 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 141.7, 140.4, 140.3, 139.1, 138.1, 133.0, 131.6, 130.0, 129.6, 129.5, 129.0, 127.3, 125.9, 118.9, 111.1, 42.5, 29.9, 22.4, 21.5.

HRMS calcd for $[M + H]^+$ $C_{25}H_{23}N_2S_2$ 415.1297, found: 415.1295.

5-(5-(4-Chlorophenyl)-2-(*p*-tolyl)thiophen-3-yl)-2-isopropyl-4-methylthiazole (29b). From 2-(2-bromo-4-methylphenyl)-5-(4-chlorophenyl)thiophene **20** (0.350 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), **29b** was isolated in 74% (0.314 g) yield as a yellow solid: mp 90–92 °C. Eluent pentane/EtOAc 80/20, R_f = 0.20.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.22 (s, 1H), 7.21 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 3.26 (sept., J = 7.6 Hz, 1H), 2.34 (s, 3H), 2.04 (s, 3H), 1.40 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5, 148.7, 141.5, 140.8, 138.0, 133.7, 132.5, 131.0, 129.6, 129.3, 128.4, 128.2, 127.6, 126.9, 124.7, 33.5, 23.3, 21.4, 15.9.

HRMS calcd for $[M + H]^+$ $C_{24}H_{23}ClNS_2$ 424.0955, found: 424.0952.

1-(4-(4-(2-Isopropyl-4-methylthiazol-5-yl)-5-(*p*-tolyl)thiophen-2-yl)phenyl)propan-1-one (30b). From 1-(4-(5-(2-bromo-4-methylphenyl)thiophen-2-yl)phenyl)propan-1-one **21** (0.371 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), **30b** was isolated in 73% (0.325 g) yield as a yellow solid: mp 120–122 °C. Eluent pentane/EtOAc 80/20, R_f = 0.27.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 8.3 Hz, 2H), 7.36 (s, 1H), 7.23 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 3.27 (sept., J = 7.6 Hz, 1H), 3.02 (q, J = 7.6 Hz, 2H), 2.35 (s, 3H), 2.05 (s, 3H), 1.40 (d, J = 7.6 Hz, 6H), 1.25 (t, J = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.1, 176.6, 148.9, 142.7, 140.6, 138.2, 138.1, 135.9, 130.9, 129.6, 129.0, 128.7, 128.3, 125.5, 124.5, 33.6, 31.9, 23.3, 21.4, 15.9, 8.5.

HRMS calcd for $[M + H]^+$ $C_{27}H_{28}NOS_2$ 446.1607, found: 446.1608.

3-(4-(2-Isopropyl-4-methylthiazol-5-yl)-5-(*p*-tolyl)thiophen-2-yl) benzonitrile (31b). From 3-(5-(2-bromophenyl)thiophen-2-yl) benzonitrile **22** (0.340 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), **31b** was isolated in 73% (0.302 g) yield as a yellow solid: mp 128–130 °C. Eluent pentane/EtOAc 80/20, R_f = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (s, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.57 (d, J = 8.3 Hz, 1H), 7.50 (t, J = 7.8 Hz, 1H), 7.30 (s, 1H), 7.21 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 3.27 (sept., J = 7.6 Hz, 1H), 2.35 (s, 3H), 2.04 (s, 3H), 1.40 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.7, 148.9, 142.7, 139.2, 138.3, 135.3, 130.9, 130.6, 130.0, 129.7, 129.6, 129.0, 128.7, 128.6, 128.3, 124.3, 118.6, 113.5, 33.5, 23.3, 21.4, 15.9.

HRMS calcd for $[M + H]^+$ $C_{25}H_{23}N_2S_2$ 415.1297, found: 415.1296.

2-(4-(2-Isopropyl-4-methylthiazol-5-yl)-5-(*p*-tolyl)thiophen-2-yl) benzonitrile (32b). From 2-(5-(2-bromophenyl)thiophen-2-yl) benzonitrile **23** (0.340 g, 1 mmol) and 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), **32b** was isolated in 76% (0.315 g) yield as a white solid: mp 130–132 °C. Eluent pentane/EtOAc 80/20, R_f = 0.30.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.3 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.39 (t, J = 7.8 Hz, 1H), 7.59 (s, 1H), 7.23 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 3.26 (sept., J = 7.6 Hz, 1H), 2.34 (s, 3H), 2.12 (s, 3H), 1.39 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 149.0, 143.6, 138.3, 137.2, 137.1, 134.6, 133.2, 131.5, 130.5, 129.6, 129.4, 128.6, 128.5, 127.8, 124.2, 118.9, 109.9, 33.5, 23.3, 21.4, 15.9.

HRMS calcd for $[M + H]^+$ $C_{25}H_{23}N_2S_2$ 415.1297, found: 415.1302.

2-Isopropyl-4-methyl-5-(5-(pyridin-3-yl)-2-(*p*-tolyl)thiophen-3-yl)thiazole (33b). The reaction of 2-(2-bromo-4-methylphenyl) thiophene **1d** (0.253 g, 1 mmol), 3-bromopyridine (0.174 g, 1.1 mmol) and KOAc (0.196 g, 2 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the corresponding 2,5-diarylated product after evaporation of the solvent and filtration on a silica plug. Then, the reaction of this crude mixture, 2-isopropyl-4-methylthiazole (0.282 g, 2 mmol), and KOAc (0.294 g, 3 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the coupling product **33b** after evaporation of the solvent and purification on silica gel in 58% (0.226 g) yield as a colorless oil. Eluent pentane/EtOAc 60/40, R_f = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (d, J = 2.4 Hz, 1H), 7.53 (dd, J = 4.8, 1.6 Hz, 1H), 7.88 (dt, J = 8.0, 1.5 Hz, 1H), 7.33 (ddd, J = 8.0, 4.8, 0.8 Hz, 1H), 7.30 (s, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 3.26 (sept., J = 7.6 Hz, 1H), 2.35 (s, 3H), 2.05 (s, 3H), 1.40 (d, J = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 148.8, 146.8, 142.4, 138.2, 138.1, 132.8, 130.8, 130.1, 129.6, 128.6, 128.4, 128.3, 124.5, 123.8, 33.5, 23.3, 21.4, 15.9.

HRMS calcd for $[M + H]^+$ $C_{23}H_{23}N_2S_2$ 391.1297, found: 391.1298.

General procedure for the preparation of 1,2-di(heteroaryl) benzenes 2a, 11a and 34a–36a

As a typical experiment, the reaction of the 2-(2-bromophenyl) thiophene derivative **1** (1 mmol), heteroarylboronic acid (2 mmol) and K_2CO_3 (0.276 g, 2 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (11.3 mg, 0.05 mmol) under argon affords the coupling product after evaporation of the solvent and purification on silica gel.

1-(5-(2-(5-Methylthiophen-2-yl)phenyl)thiophen-2-yl)ethan-1-one (2a). From 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol) and (5-acetylthiophen-2-yl)boronic acid (0.340 g, 2 mmol), **2a** was obtained in 61% (0.182 g) yield as a yellow oil. Eluent pentane, R_f = 0.30.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 3.9 Hz, 1H), 7.50–7.46 (m, 2H), 7.42–7.32 (m, 2H), 6.88 (d, J = 3.9 Hz, 1H), 6.64 (d, J = 3.5 Hz, 1H), 6.61 (d, J = 3.5 Hz, 1H), 2.53 (s, 3H), 2.45 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 152.0, 144.2, 141.1, 139.6, 134.4, 132.8, 132.6, 131.4, 131.0, 129.0, 128.3, 127.9, 127.4, 125.6, 26.8, 15.5.

HRMS calcd for $[M + H]^+$ $C_{17}H_{15}OS_2$ 299.0559, found: 299.0558.

2-Methyl-5-(2-(thiophen-2-yl)phenyl)thiophene (34a). From 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol) and 2-thienylboronic acid (0.256 g, 2 mmol), **34a** was obtained in 80% (0.205 g) yield as a colorless oil. Eluent pentane, R_f = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.45 (m, 2H), 7.39–7.31 (m, 2H), 7.28 (dd, J = 5.1, 1.2 Hz, 1H), 6.98 (dd, J = 5.1, 3.5 Hz, 1H), 6.93 (dd, J = 3.5, 1.2 Hz, 1H), 6.67 (d, J = 3.8 Hz, 1H), 6.61 (d, J = 3.8 Hz, 1H), 2.46 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 140.7, 140.4, 134.4, 133.7, 131.2, 131.0, 128.0, 127.7, 127.2, 127.1, 127.0, 126.0, 125.3, 15.4.

HRMS calcd for $[M + H]^+$ $C_{15}H_{13}S_2$ 257.0453, found: 257.0453.

5-(2-(5-Methylthiophen-2-yl)phenyl)thiophene-2-carbaldehyde (35a). From 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol) and (5-formylthiophen-2-yl)boronic acid (0.312 g, 2 mmol), **35a** was obtained in 41% (0.116 g) yield as a yellow oil. Eluent pentane/EtOAc 80/20, R_f = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86 (s, 1H), 7.62 (d, J = 3.9 Hz, 1H), 7.52–7.47 (m, 2H), 7.44–7.34 (m, 2H), 6.98 (d, J = 3.9 Hz, 1H), 6.64 (d, J = 3.5 Hz, 1H), 6.61 (d, J = 3.5 Hz, 1H), 2.45 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 183.1, 153.6, 143.7, 141.3, 139.4, 136.4, 134.5, 132.5, 131.5, 130.9, 129.3, 128.5, 128.0, 127.5, 125.6, 15.4.

HRMS calcd for $[M + H]^+$ $C_{16}H_{13}OS_2$ 285.0402, found: 285.0400.

2-Chloro-5-(2-(thiophen-2-yl)phenyl)thiophene (36a). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.271 g, 1 mmol) and 2-thienylboronic acid (0.256 g, 2 mmol), **36a** was obtained in 91% (0.252 g) yield as a yellow oil. Eluent pentane, R_f = 0.33.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.43 (m, 2H), 7.40–7.33 (m, 2H), 7.31 (dd, J = 5.1, 1.2 Hz, 1H), 7.00 (dd, J = 5.1, 3.5 Hz, 1H), 6.93 (dd, J = 3.5, 1.2 Hz, 1H), 6.77 (d, J = 3.8 Hz, 1H), 6.68 (d, J = 3.8 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 142.2, 141.5, 133.8, 133.2, 131.4, 130.9, 130.4, 128.4, 128.2, 127.5, 127.2, 126.4, 126.3, 126.2.

HRMS calcd for $[M + H]^+$ $C_{14}H_{10}ClS_2$ 276.9907, found: 276.9909.

4-(2-(5-Chlorothiophen-2-yl)phenyl)-3,5-dimethylisoxazole (11a). From 2-(2-bromophenyl)-5-chlorothiophene **1c** (0.271 g, 1 mmol) and (3,5-dimethylisoxazol-4-yl)boronic acid (0.282 g, 2 mmol), **11a** was obtained in 58% (0.168 g) yield as a yellow oil. Eluent pentane/EtOAc 80/20, R_f = 0.30.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, J = 7.8 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 7.8 Hz, 1H), 6.78 (d, J = 3.8 Hz, 1H), 6.69 (d, J = 3.8 Hz, 1H), 2.18 (s, 3H), 1.95 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 159.5, 140.9, 134.3, 132.1, 130.8, 129.8, 129.0, 128.3, 128.0, 126.4, 125.5, 116.0, 11.4, 10.5.

HRMS calcd for $[M + H]^+$ $C_{15}H_{13}ClNOS$ 290.0401, found: 290.0402.

2,5-Dimethylnaphtho[1,2-*b*:3,4-*b*′]dithiophene (37). The reaction of 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol), 4-bromo-2-methylthiophene (0.354 g, 2 mmol), and KOAc (0.294 g, 3 mmol) at 150 °C for 48 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the coupling product after evaporation of the solvent and purification on silica gel **37** in 35% (0.094 g) yield as a white solid: mp 138–140 °C. Eluent pentane, R_f **37** = 0.20, R_f **38** = 0.23.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30–8.25 (m, d1H), 8.10–8.04 (m, 1H), 7.65 (q, J = 1.2 Hz, 1H), 7.58–7.51 (m, 2H), 7.23 (q, J = 1.2 Hz, 1H), 2.73 (d, J = 1.2 Hz, 3H), 2.71 (d, J = 1.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 138.4, 134.7, 133.1, 132.6, 132.0, 127.3, 126.8, 125.7, 125.5, 124.7, 124.2, 120.8, 120.7, 16.3, 16.2.

HRMS calcd for $[M + H]^+$ $C_{16}H_{13}S_2$ 269.0453, found: 296.0456.

The intermediate 3-bromo-5,5′-dimethyl-2′-phenyl-2,3′-bithiophene **38** was also isolated in a low yield in an impure form as a colorless oil:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.21 (m, 5H), 6.82 (q, J = 1.2 Hz, 1H), 6.63 (q, J = 1.2 Hz, 1H), 2.52 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.2, 138.2, 134.4, 131.4, 129.3, 128.7, 128.6, 128.5, 128.2, 127.4, 108.9, 15.6, 15.5.

HRMS calcd for $[M + H]^+$ $C_{16}H_{14}BrS_2$ 348.9715, found: 348.9717.

2,6-Dimethyl-4-phenylnaphtho[1,2-*b*:3,4-*c*′]dithiophene (39). The reaction of 2-(2-bromophenyl)-5-methylthiophene **1a** (0.253 g, 1 mmol) and KOAc (0.294 g, 3 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the coupling product after evaporation of the solvent and purification on silica gel **39** in 65% (0.112 g) yield as a white solid: mp 172–174 °C. Eluent pentane, R_f = 0.13.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.8, 2.0 Hz, 1H), 7.61–7.53 (m, 2H), 7.53–7.40 (m, 5H), 6.64 (q, J = 1.3 Hz, 1H), 3.06 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 138.7, 135.7, 135.6, 132.4, 132.3, 131.3, 130.7, 129.2, 128.8, 128.7, 128.6, 128.4, 126.4, 126.1, 125.5, 124.0, 123.3, 18.4, 16.2.

HRMS calcd for $[M + H]^+$ $C_{22}H_{17}S_2$ 345.0766, found: 345.0767.

4-(3,4-Dimethylphenyl)-2,6,8,9-tetramethylnaphtho[1,2-*b*:3,4-*c*′]dithiophene (40). The reaction of 2-(2-bromo-4,5-dimethylphenyl)-5-methylthiophene **1e** (0.281 g, 1 mmol) and KOAc (0.294 g, 3 mmol) at 150 °C for 16 h in DMA (4 mL) in the presence of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) under argon affords the coupling product after evaporation of the solvent and purification on silica gel **40** in 51% (0.102 g) yield as a white solid: mp 102–104 °C. Eluent pentane, R_f = 0.17.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8. 15 (s, 1H), 7.60 (s, 1H), 7.34 (s, 1H), 7.30 (d, J = 7.0 Hz, 1H), 7.22 (d, J = 7.0 Hz, 1H), 6.73 (q, J = 1.3 Hz, 1H), 3.04 (s, 3H), 2.45 (s, 3H), 2.43 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 136.7, 136.6, 135.3, 135.0, 134.7, 132.9, 132.2, 131.8, 130.8, 130.5, 130.4, 129.8, 129.1, 128.5, 126.9, 126.8, 126.1, 124.5, 123.3, 20.7, 20.0, 19.9, 19.8, 18.2, 16.1.

HRMS calcd for $[M + H]^+$ $C_{26}H_{25}S_2$ 401.1392, found: 401.1393.

Conflicts of interest

There are no conflicts to declare.

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