Intermolecular Followed by Intramolecular Palladium-Catalyzed Direct Arylations for the Synthesis of π-Extended Aromatic Compounds Containing One or Two Heteroelements

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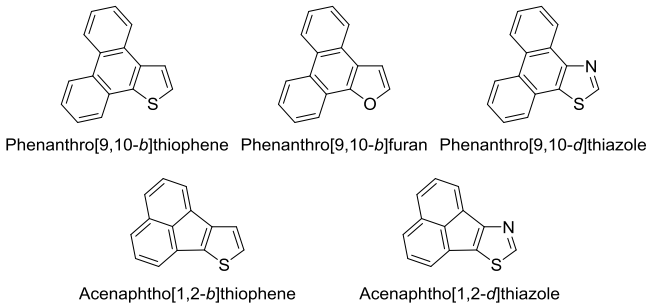
Abstract: Herein, we report that palladium-catalyzed C-H bond activation can overcome some of the challenges in the preparation of π-extended aromatics containing one or two heteroelements, which are important structures in organic material science. The sequential palladium-catalyzed intermolecular direct C5-arylation of heteroarenes by aryl bromides, followed by bromination of the heteroarene unit with *N*-bromosuccinimide, and finally palladium-catalyzed intramolecular direct arylation allowed the synthesis of the desired phenanthro[9,10-*b*]thiophenes, phenanthro[9,10-*b*]furans, phenanthro[9,10-*b*]thiazoles, acenaphtho[1,2-*d*]thiophenes and acenaphtho[1,2-*d*]thiazoles in only three steps.

Key topic: C-H bond functionalization

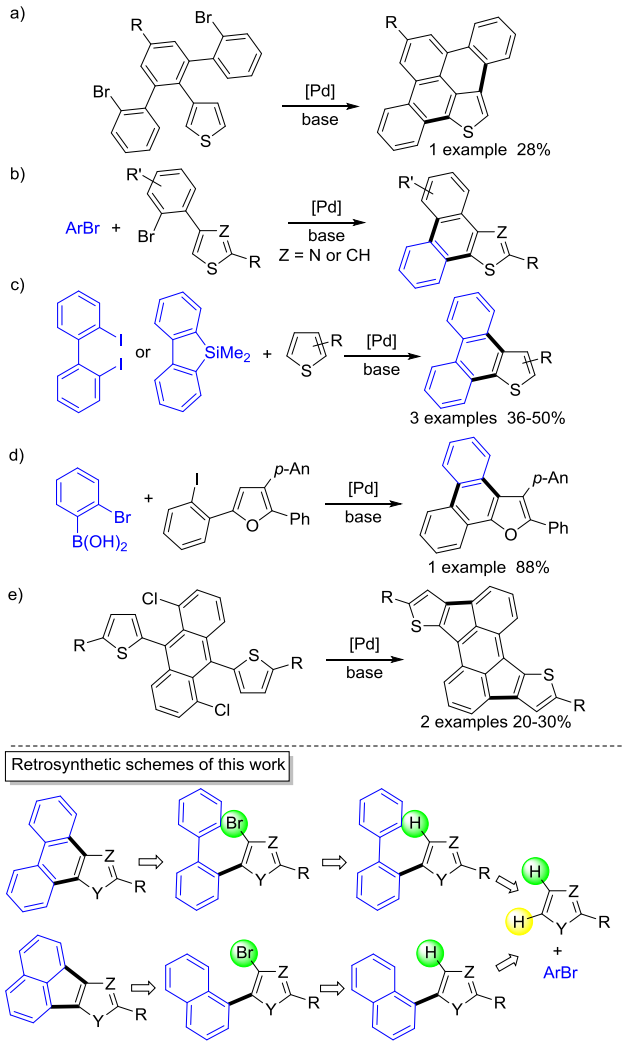
Introduction

The synthesis of π-extended polycyclic heteroaromatic hydrocarbons is currently a very hot topic in organic material science, as the introduction of heteroelements in these π-extended structures often induces a modification of their chemical and/or physical properties. For example, they are employed for the preparation of optoelectronic devices such as organic field-effect transistors (OFETs).[1] Their unique properties are directly linked to their structures. However, the synthesis of such compounds often suffers from low functional group tolerance and/or tedious access to the key intermediates due to multi-step synthesis. Palladium-catalyzed direct functionalization through C-H bond cleavage[2-4] can overcome some of the challenges in the preparation of such materials. [5-9] Indeed, the recent remarkable progress in the direct arylation of heteroaromatics or arenes has set the stage for the synthesis of complex molecules using sequential C-H bond activation/arylations. Such transformations appear as one of the most suitable methods in terms of i) number of synthetic steps, ii) functional group tolerance, iii) respect of the environment (only the formation of HX associated with a base as side product and no requirement to prepare and use sensitive organometallic reagents).
To our knowledge, only a few examples dealing with the synthesis of phenanthro[9,10-*b*]thiophenes,[5] phenanthro[9,10-*b*]thiazoles,[6] phenanthro[9,10-*b*]furans,[7] acenaphtho[1,2-*d*]thiophenes[8] (Scheme 1) *via* Pd-catalyzed C-H bond activation have been reported so far, and no examples of preparation of acenaphtho[1,2-*d*]thiazoles has been described.



Scheme 1. Structures of some π-extended heteroaromatics.

In 2004 Höger *et al.* employed Pd-catalyzed C2- and C4-intramolecular direct arylations of a thiophene bearing a 2,5-dibromophenyl group at C3 position for the preparation of a phenanthro[9,10-*b*]thiophene derivative in 28% yield (Scheme 2, a).[5a] In 2015, Kanai, Kuninobu *et al.* prepared a benzo[*b*]phenanthro[9,10-*d*]thiophene from a benzothiophene substituted by an *ortho*-biphenyl group at C3 position *via* Pd-catalyzed oxidative C-H/C-H coupling reaction.[5b] Then, in 2016 and 2017, our group reported the synthesis of phenanthro[9,10-*b*]thiophenes and phenanthro[9,10-*b*]thiazoles from thiophenes and thiazoles bearing 2-bromoaryl groups at the C4 position, *via* C5 arylations followed by an intramolecular cyclization (Scheme 2, b).[5c,6] In 2017, using a diiodobiphenyl as π-extending agent, Itami *et al.* produced a phenanthro[9,10-*b*]thiophene in one step;[5d,5e] whereas, Miao *et al.* employed dibenzosiloles as π-extending agents (Scheme 2, c).[5f] A single example of synthesis of a phenanthro[9,10-*b*]furan *via* a domino Suzuki−Miyaura coupling/intramolecular direct arylation using 2-bromophenylboronic acid has been described by Yoshikai *et al.* in 2014 (Scheme 2, d).[7c] By contrast, the preparation of acenaphtho[1,2-*d*]thiophene *via* C-H bond activation remain scarce.[8] The first example, which was reported in 1999 by Dehaen's group, deals with the ring closure of the 1,5-dichloro-9,10-diarylanthracenes to produce the corresponding thiophene rubicene analogs (Scheme 2, e).[8a]



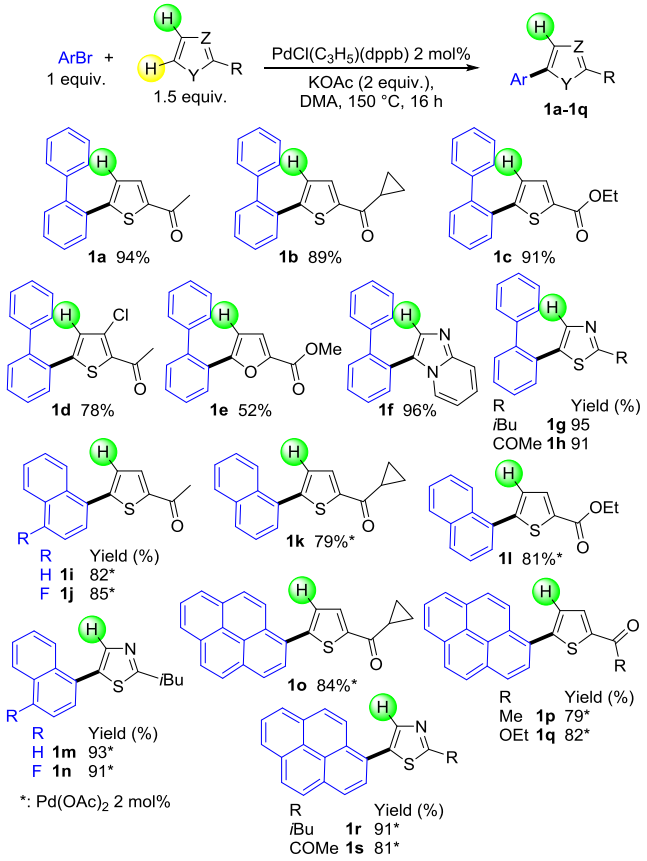
Scheme 2. Synthesis of O- or S-containing π-extended aromatics *via* a C-H bond activation step using thiophenes, furans or thiazoles.

Herein, we report on the potential of sequential intermolecular Pd-catalyzed direct C5-arylation of heteroaromatics, regioselective C4-bromination of the heteroarene unit, and intramolecular Pd-catalyzed direct arylation for the synthesis π-extended polycyclic heteroaromatic hydrocarbons.

Results and Discussion

First, we studied the C5-arylation of a set of heteroarenes with 2-bromobiphenyl using our previously reported reaction conditions (e.g., 2 mol% $PdCl(C_3H_5)(dppb)$ catalyst, KOAc as the base in DMA at 150 °C) (Scheme 3).[10] Under these conditions, thiophene derivatives bearing acetyl, cyclopropylmethanone or ester C2-substituents gave the expected arylated products **1a**-**1c** in 89-94% yields. A slightly lower yield of 78% in **1d** was obtained for the reaction of 2-acetyl-3-chlorothiophene with 2-bromobiphenyl. The reactions of 2-bromobiphenyl with a furan derivative, imidazo[1,2-*a*]pyridine and thiazole derivatives were also successful giving rise to the products **1e**-**1h** in 52-96% yields. Then, we introduced a 1-naphthyl C5-substituent on thiophene and thiazole derivatives using the same reaction conditions, with the exception of the catalyst which was replaced by $Pd(OAc)_2$, as it is known that the oxidative addition of 1-bromonaphthalene proceeds nicely with this phosphine-free catalyst.[11]

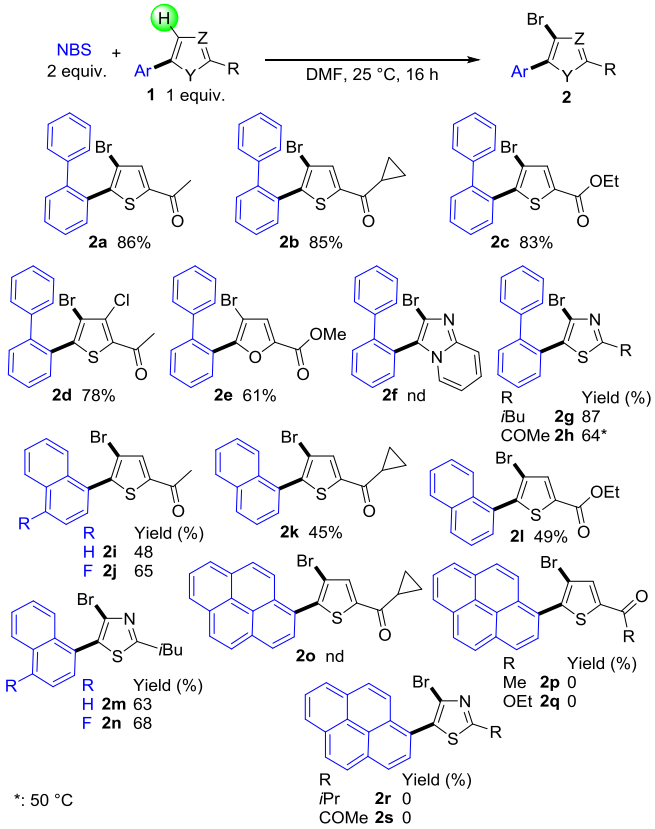
In all cases, the expected products **1i** and **1k**-**1m** were obtained in high yields. Similar yields were obtained for the reactions of 2-acetylthiophene and 2-isobutylthiazole with 1-bromo-4-fluoronaphthalene affording **1j** and **1n** in 85% and 91% yield, respectively. 1-Bromopyrene was also employed as the aryl source using thiophene and thiazole derivatives as reaction partners. In all cases, using again 2 mol% of $Pd(OAc)_2$ catalyst, the expected pyren-1-yl-substituted heteroarenes **1o**-**1s** were obtained in high yields.



Scheme 3. Pd-catalyzed direct C5-arylations of heteroarenes with 2-bromobiphenyl, 1-bromonaphthalenes and 1-bromopyrene.

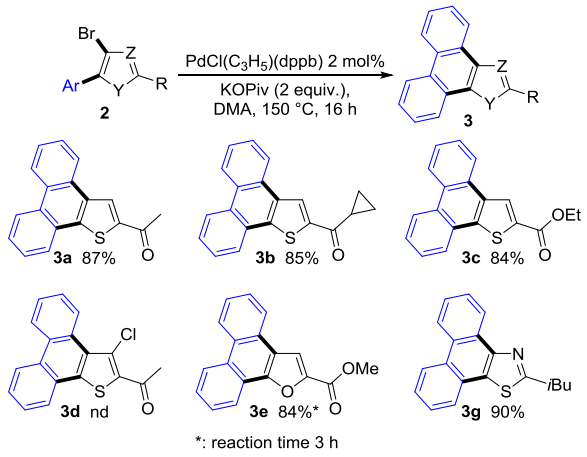
Then, the reactivity of the fifteen C5-arylated heteroarenes **1a**-**1o** in bromination reaction using *N*-bromosuccinimide (NBS) as easy to handle bromine source was investigated (Scheme 4). As the biphenyl-substituted thiophenes **1a**-**1c** contain two C-H bonds on the thiophene ring, mixtures of brominated products might have been obtained. However, a few reports indicate that from thiophene derivatives bearing an electron-withdrawing substituent at C2-position and an alkyl or an aryl at C5-position, the bromination mostly occurred at the C4-position; whereas, the C-H bond at the C3-position remained untouched.[12] To our delight, the desired 4-bromo-substituted thiophene derivatives **2a**-**2c** were obtained in high regioselectivities and in 83-86% yields. A good yield in 4-bromothiophene derivative **2d** was also obtained for the bromination of **1d** which contained an additional chloro-C3-substituent compared to **1a**. The C4-bromination of the furan ring[13a] of **1e** was also successful affording regioselectively **2e** in 61% yield. From the imidazo[1,2-*a*]pyridine derivative **1f** and NBS at 25 or 70 °C, no formation of the products **2f** was observed by GC/MS analysis of the crude mixtures, and **1f** was recovered. To our knowledge, the bromination of the 5-membered ring of imidazo[1,2-*a*]pyridine derivatives has been rarely described.[13b] This result might come from an unfavorable combination of electronic and steric properties. Conversely, the bromination of the C4-position of the

thiazole rings[14] of **1g** and **1h** proceeded nicely affording the expected products **2g** and **2h** in 87% and 64% yield, respectively. The naphthyl-substituted thiophenes **1i**, **1k** and **1l** treated by NBS gave the desired products **2i**, **2k** and **2l** in moderate yields, due to the moderate regioselectivities of these reactions. Moreover, their purification by silica chromatography afforded the expected products contaminated with unidentified side-products. The bromination of 1-(5-(4-fluoronaphthalen-1-yl)thiophen-2-yl)ethan-1-one **1j** was more selective affording the desired product **2j** in 65% yield in pure form. The 5-naphthylthiazoles **1m** and **1n** were also successfully brominated, and the desired products **2m** and **2n** were isolated in 63% and 68% yield, respectively. It should be mentioned that the pyrene-substituted thiophenes **2o**-**2q** and thiazoles **2r** and **2s** could not be isolated from **1o**-**1s**, as several unidentified products were formed in the course of these bromination reactions.



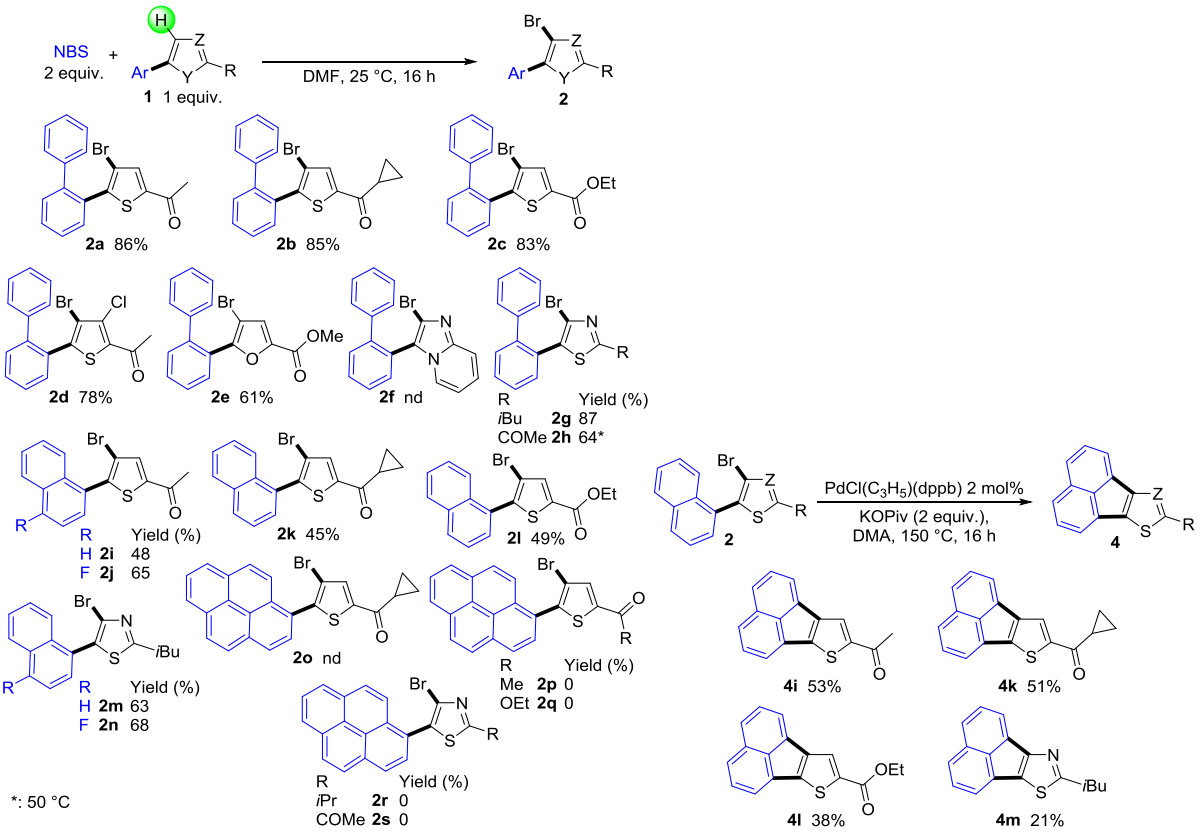
Scheme 4. C4-brominations of the C5-arylated heteroarenes **1a**-**1s**.

Finally, we investigated the Pd-catalyzed intramolecular C-H bond arylations of **2a**-**2h** and **2i**-**2n** (Schemes 5 and 6). We tested similar conditions employed for the C5-arylations of heteroarenes of scheme 3 – namely 2 mol% of $PdCl(C_3H_5)(dppb)$ in DMA at 150 °C – with 2 equiv. of PivOK as the base instead of KOAc, as it was previously demonstrated that this base is very effective to promote the C-H bond cleavage of benzene derivatives.[6] The intramolecular arylations of **2a**-**2c** proceeded faster than the intermolecular reactions affording the desired phenanthro[9,10-*b*]thiophenes **3a**-**3c** in 84-87% yields. The presence of a chloro-substituent at C3-position on the thiophene ring had a deleterious influence as no formation of product **3d** was detected from **2d**. Part of the starting material **2d** was recovered and degradation products were also observed. The intramolecular C-H bond arylation of the furan derivative **1e** proceeded nicely delivering the phenanthro[9,10-*b*]furan **2e** in 84% yield. A very clean cyclization reaction was also observed with the 4-bromothiazole derivative **2g** affording the phenanthro[9,10-*b*]thiazole **3g** in 90% yield. Conversely, the cyclisation of **2h** was not successful, and only degradation products were obtained.



Scheme 5. Pd-catalyzed direct intramolecular arylations of bromo-substituted heteroarenes **2a**-**2h**.

To our knowledge, the synthesis of acenaphtho[1,2-*b*]thiophenes has rarely been described[8,15] and only one example of preparation of a acenaphtho[1,2-*d*]thiazole has been reported.[16] Again, we employed 2 mol% of $PdCl(C_3H_5)$(dppb) with 2 equiv. of PivOK as base/ligand in DMA to promote the cyclization of the 5-naphthylthiophenes **2i**-**2n** (Scheme 6). The desired acenaphtho[1,2-*b*]thiophenes **4i**, **4k** and **4l** were only obtained in 38-53% yields, from **2i**, **2k** and **2l** due to the formation of degradation side-products. Unexpectedly, no formation of the expected acenaphtho[1,2-*b*]thiophene was observed in GC/MS of the crude mixture using the fluoro-substituted 5-naphthylthiophene **2j**. In the course of this reaction, a complete conversion of **2j** was observed, but only unidentified side-products were formed. The Pd-catalyzed annulation using 5-naphthylthiazole **2m** was moderately successful, as the desired acenaphtho[1,2-*d*]thiazole **4m** was only obtained in 21% yield. With 4-bromo-5-(4-fluoronaphthalen-1-yl)-2-isobutylthiazole **2n**, a mixture of starting material and debrominated compound **1n** was obtained; whereas, the expected acenaphtho[1,2-*d*]thiazole was not detected.



Scheme 6. Pd-catalyzed direct intramolecular arylations of the 4-bromo-substituted heteroarenes **2i**-**2n**.

Conclusions

In summary, we have investigated the potential of the intermolecular Pd-catalyzed direct C5-arylation of heteroaromatics followed by their regioselective C4-bromination and intramolecular Pd-catalyzed annulation reaction for the synthesis of π-extended aromatic compounds containing heteroelements. With most heteroaromatics, the first step proceeded in high yields using 2-bromobiphenyl, 1-bromonaphthalene or 1-bromopyrene as aryl sources and 2 mol% of $PdCl(C_3H_5)(dppb)$ as air-stable catalyst associated to KOAc as inexpensive base. The resulting coupling products were submitted to C4-bromination reactions of the heteroarene unit using *N*-bromosuccinimide as bromination agent. Both biphenyl- and naphthyl-substituted thiophenes and thiazoles were regioselectively brominated affording the target products; whereas, pyrene-substituted heteroarenes gave complex mixtures of products. Finally, the intramolecular Pd-catalyzed annulation reaction afforded the π-extended aromatic compounds with phenanthro[9,10-*b*]thiophene, phenanthro[9,10-*b*]furan, phenanthro[9,10-*b*]thiazole, acenaphtho[1,2-*d*]thiophene or acenaphtho[1,2-*d*]thiazole skeletons in low to high yields. Therefore, this synthetic pathway should overcome some of the challenges in the preparation of π-extended heteroaromatics containing one or two heteroelements useful in organic material science.

Experimental Section

All reactions were carried out under argon atmosphere with standard Schlenk techniques. DMA was purchased from Acros Organics and was not purified before use. ^{1}H NMR spectra were recorded on Bruker GPX (400 MHz) spectrometer. Chemical shifts (δ) were reported in parts per million relative to residual chloroform (7.28 ppm for ^{1}H; 77.0 ppm for ^{13}C), constants were reported in Hertz. ^{1}H NMR

assignment abbreviations were the following: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). ^{13}C NMR spectra were recorded at 100 MHz on the same spectrometer and reported in ppm. All reagents were weighed and handled in air.

Preparation of the $PdCl(C_3H_5)$(dppb) catalyst:[17] An oven-dried 40 mL Schlenk tube equipped with a magnetic stirring bar under 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 were added, then, the solution was stirred at room temperature for twenty minutes. The solvent was removed in vacuum. The powder was used without purification. (^{31}P 381 MHz, $CDCl_3$) δ = 19.3 (s).

Procedure A (Direct intermolecular arylation of heteroarenes): To a 25 mL oven dried Schlenk tube, aryl bromide (1 mmol), heteroarene derivative (1.5 mmol), KOAc (0.196 g, 2 mmol), DMA (2 mL) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol) or $Pd(OAc)_2$ (4.4 mg, 0.02 mmol) (see scheme) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 150 °C (oil bath temperature) for 16 hours. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography (diethyl ether:heptane 1:9) to afford the desired arylated products **1a**-**1r**.

1-(5-([1,1'-Biphenyl]-2-yl)thiophen-2-yl)ethan-1-one (1a)

Following the procedure **A**, from 2-acetylthiophene (0.189 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1a** was obtained in 94% yield (0.261 g) as a white solid: mp 109-111 °C.

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.61-7.56 (m, 1H), 7.49-7.40 (m, 4H), 7.36-7.31 (m, 3H), 7.29-7.25 (m, 2H), 6.65 (d, *J* = 3.9 Hz, 1H), 2.50 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.5, 152.1, 143.7, 141.2, 140.9, 132.6, 132.2, 131.1, 130.5, 129.4, 129.0, 128.3, 128.2, 127.9, 127.4, 26.6.

Elemental analysis: calcd (%) for $C_{18}H_{14}OS$ (278.37): C 77.67, H 5.07; found: C 77.92, H 5.02.

(5-([1,1'-Biphenyl]-2-yl)thiophen-2-yl)(cyclopropyl)methanone (1b) Following the procedure **A**, from cyclopropyl(thiophen-2-yl)methanone (0.228 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1b** was obtained in 89% yield (0.270 g) as a white solid: mp 128-130 °C.

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63-7.60 (m, 1H), 7.59 (d, *J* = 3.9 Hz, 1H), 7.50-7.40 (m, 3H), 7.40-7.25 (m, 5H), 6.68 (d, *J* = 3.9 Hz, 1H), 2.53-2.45 (m, 1H), 1.30-1.25 (m, 2H), 1.05-0.99 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.7, 151.6, 144.2, 141.2, 141.0, 132.3, 131.7, 131.1, 130.6, 129.6, 128.9, 128.4, 127.8, 127.4, 17.8, 11.4.

Elemental analysis: calcd (%) for $C_{20}H_{16}OS$ (304.41): C 78.91, H 5.30; found: C 79.14, H 5.39.

Ethyl 5-([1,1'-biphenyl]-2-yl)thiophene-2-carboxylate (1c)

Following the procedure **A**, from ethyl thiophene-2-carboxylate (0.234 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1c** was obtained in 91% yield (0.280 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63-7.57 (m, 2H), 7.39-7.34 (m, 3H), 7.34-7.27 (m, 5H), 6.67 (d, *J* = 3.9 Hz, 1H), 4.38 (q, *J* = 7.6 Hz, 2H), 1.40 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.2, 150.5, 141.2, 140.9, 133.3, 132.3, 131.1, 130.6, 129.6, 128.8, 128.3, 127.9, 127.8, 127.4, 61.1, 14.5.

Elemental analysis: calcd (%) for $C_{19}H_{16}O_2S$ (308.40): C 74.00, H 5.23; found: C 73.78, H 4.98.

1-(5-([1,1'-Biphenyl]-2-yl)-3-chlorothiophen-2-yl)ethan-1-one (1d)

Following the procedure **A**, from 1-(3-chlorothiophen-2-yl)ethan-1-one (0.240 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1d** was obtained in 78% yield (0.243 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.58-7.52 (m, 1H), 7.50-7.38 (m, 3H), 7.38-7.33 (m, 3H), 7.28-7.23 (m, 2H), 6.58 (s, 1H), 2.61 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 189.7, 149.5, 141.2, 140.3, 137.0, 131.2, 131.1, 130.1, 130.0, 129.5, 129.4, 128.5, 128.0, 127.9, 127.7, 29.6.

Elemental analysis: calcd (%) for $C_{18}H_{13}ClOS$ (312.81): C 69.11, H 4.19; found: C 69.30, H 4.28.

Methyl 5-([1,1'-biphenyl]-2-yl)furan-2-carboxylate (1e)

Following the procedure **A**, from methyl furan-2-carboxylate (0.189 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1e** was obtained in 52% yield (0.144 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.96 (d, *J* = 7.4 Hz, 1H), 7.47-7.34 (m, 5H), 7.34-7.24 (m, 3H), 6.97 (d, *J* = 3.6 Hz, 1H), 5.56 (d, *J* = 3.6 Hz, 1H), 3.88 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.2, 156.5, 142.9, 141.4, 140.4, 130.8, 129.1, 128.6, 128.4, 127.7, 127.5, 119.5, 111.1, 51.8.

Elemental analysis: calcd (%) for $C_{18}H_{14}O_3$ (278.31): C 77.68, H 5.07; found: C 77.52, H 4.88.

3-([1,1'-Biphenyl]-2-yl)imidazo[1,2-*a*]pyridine (1f)

Following the procedure **A**, from imidazo[1,2-*a*]pyridine (0.177 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1f** was obtained in 96% yield (0.259 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.52 (s, 1H), 7.51-7.33 (m, 6H), 7.14-6.98 (m, 5H), 6.91-6.86 (m, 1H), 6.31 (t, *J* = 6.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 145.3, 141.5, 140.5, 133.6, 131.9, 130.6, 129.3, 128.3, 127.9, 127.8, 127.2, 127.1, 124.9, 123.8, 123.4, 117.5, 111.5.

Elemental analysis: calcd (%) for $C_{19}H_{14}N_2$ (270.34): C 84.42, H 5.22; found: C 84.59, H 5.00.

5-([1,1'-Biphenyl]-2-yl)-2-isobutylthiazole (1g)

Following the procedure **A**, from 2-isobutylthiazole (0.211 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1g** was obtained in 95% yield (0.278 g) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.57-7.52 (m, 1H), 7.43 (s, 1H), 7.41-7.38 (m, 3H), 7.34-7.30 (m, 3H), 7.30-7.23 (m, 2H), 2.78 (d, *J* = 7.6 Hz, 2H), 2.11-2.00 (m, 1H), 0.97 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.5, 141.3, 140.9, 140.5, 137.2, 130.6, 130.4, 130.2, 129.7, 128.3, 128.2, 127.7, 127.3, 42.2, 29.8, 22.3.

Elemental analysis: calcd (%) for $C_{19}H_{19}NS$ (293.43): C 77.77, H 6.53; found: C 77.59, H 6.35.

1-(5-([1,1'Biphenyl]-2-yl)thiazol-2-yl)ethan-1-one (1h)

Following the procedure **A**, from 2-acetylthiazole (0.190 g, 1.5 mmol), 2-bromobiphenyl (0.233 g, 1 mmol) and $PdCl(C_3H_5)$(dppb) (12.2 mg, 0.02 mmol), compound **1h** was obtained in 91% yield (0.254 g) as a white solid mp 117-119 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.57 (s, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.50-7.38 (m, 3H), 7.34-7.30 (m, 3H), 7.23-7.17 (m, 2H), 2.64 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.7, 166.1, 146.1, 143.3, 141.7, 140.2, 131.0, 130.7, 129.5, 129.4, 129.0, 128.5, 127.9, 127.8, 25.7.

Elemental analysis: calcd (%) for $C_{17}H_{13}NOS$ (279.36): C 73.09, H 4.69; found: C 73.25, H 4.47.

1-(5-(Naphthalen-1-yl)thiophen-2-yl)ethan-1-one (1i)

Following the procedure **A**, from 2-acetylthiophene (0.189 g, 1.5 mmol), 1-bromonaphthalene (0.207 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1i** was obtained in 82% yield (0.206 g) as a white solid: mp 113-115 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.21 (d, *J* = 8.2 Hz, 1H), 7.97-7.90 (m, 2H), 7.79 (d, *J* = 3.8 Hz, 1H), 7.63-7.50 (m, 4H), 7.30 (d, *J* = 3.8 Hz, 1H), 2.65 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.7, 150.7, 144.2, 133.8, 132.7, 131.4, 131.3, 129.5, 128.5, 128.4, 128.3, 126.9, 126.3, 125.2, 26.7.

Elemental analysis: calcd (%) for $C_{16}H_{12}OS$ (252.33): C 76.16, H 4.79; found: C 76.34, H 4.62.

1-(5-(4-Fluoronaphthalen-1-yl)thiophen-2-yl)ethan-1-one (1j)

Following the procedure **A**, from 2-acetylthiophene (0.189 g, 1.5 mmol), 1-bromo-4-fluoronaphthalene (0.225 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1j** was obtained in 85% yield (0.229 g) as a white solid: mp 167-169 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.23-8.14 (m, 2H), 7.79-7.75 (m, 1H), 7.64-7.56 (m, 2H), 7.55-7.49 (m, 1H), 7.28-7.17 (m, 2H), 2.61 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.6, 159.2 (d, *J* = 255.5 Hz), 149.9, 144.3, 132.7, 132.6, 128.5, 128.2 (d, *J* = 8.6 Hz), 127.8, 127.6 (d, *J* = 4.5 Hz), 126.6 (d, *J* = 1.9 Hz), 125.3 (d, *J* = 2.3 Hz), 124.0 (d, *J* = 16.3 Hz), 121.0 (d, *J* = 5.6 Hz), 109.0 (d, *J* = 20.5 Hz), 26.7.

Elemental analysis: calcd (%) for $C_{16}H_{11}FOS$ (270.32): C 71.09, H 4.10; found: C 71.25, H 4.32.

Cyclopropyl(5-(naphthalen-1-yl)thiophen-2-yl)methanone (1k)

Following the procedure **A**, from cyclopropyl(thiophen-2-yl)methanone (0.228 g, 1.5 mmol), 1-bromonaphthalene (0.207 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1k** was obtained in 79% yield (0.220 g) as a white solid: mp 162-164 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.24 (d, *J* = 8.2 Hz, 1H), 7.97-7.90 (m, 3H), 7.63 (dd, *J* = 7.1, 1.0 Hz, 1H), 7.62-7.50 (m, 3H), 7.32 (d, *J* = 3.8 Hz, 1H), 2.68-2.56 (m, 1H), 1.38-1.30 (m, 2H), 1.14-1.05 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 150.1, 144.6, 133.9, 131.7, 131.3, 129.4, 128.5, 128.4, 128.3, 126.9, 126.3, 125.3, 125.2, 18.0, 11.4.

Elemental analysis: calcd (%) for $C_{18}H_{14}OS$ (278.37): C 77.67, H 5.07; found: C 77.62, H 5.00.

Ethyl 5-(naphthalen-1-yl)thiophene-2-carboxylate (1l)[18]

Following the procedure **A**, from ethyl thiophene-2-carboxylate (0.234 g, 1.5 mmol), 1-bromonaphthalene (0.207 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1l** was obtained in 81% yield (0.228 g) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.25 (d, *J* = 8.2 Hz, 1H), 7.97-7.88 (m, 3H), 7.61 (dd, *J* = 7.1, 1.1 Hz, 1H), 7.59-7.51 (m, 2H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.26 (d, *J* = 3.8 Hz, 1H), 4.48 (q, *J* = 7.6 Hz, 2H), 1.47 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.3, 149.0, 133.9, 133.7, 133.6, 131.5, 131.4, 129.4, 128.6, 128.3, 128.1, 126.9, 126.3, 125.3, 125.2, 61.3, 14.5.

2-Isobutyl-5-(naphthalen-1-yl)thiazole (1m)

Following the procedure **A**, from 2-isobutylthiazole (0.211 g, 1.5 mmol), 1-bromonaphthalene (0.207 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1m** was obtained in 93% yield (0.248 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.19 (d, *J* = 8.2 Hz, 1H), 7.91-7.81 (m, 3H), 7.57-7.47 (m, 3H), 7.45 (t, *J* = 7.6 Hz, 1H), 2.98 (d, *J* = 7.6 Hz, 2H), 2.32-2.17 (m, 1H), 1.11 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.5, 141.2, 135.5, 133.8, 131.9, 129.0 (m), 128.6, 128.5, 126.8, 126.2, 125.3, 125.2, 42.5, 29.9, 22.5.

Elemental analysis: calcd (%) for $C_{17}H_{17}NS$ (267.39): C 76.36, H 6.41; found: C 76.50, H 6.65.

5-(4-Fluoronaphthalen-1-yl)-2-isobutylthiazole (1n)

Following the procedure **A**, from 2-isobutylthiazole (0.211 g, 1.5 mmol), 1-bromo-4-fluoronaphthalene (0.225 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1n** was obtained in 91% yield (0.259 g) as a white solid: mp 109-111 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.03-7.95 (m, 2H), 7.62 (s, 1H), 7.42-7.35 (m, 2H), 7.28 (dd, *J* = 7.9, 5.4, 1H), 6.97 (dd, *J* = 10.0, 7.9 Hz, 1H), 2.84 (d, *J* = 7.6 Hz, 2H), 2.20-2.00 (m, 1H), 0.98 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.5, 158.7 (d, *J* = 254.8 Hz), 141.2, 134.6, 133.1 (d, *J* = 4.9 Hz), 128.3 (d, *J* = 8.6 Hz), 127.5, 126.4 (d, *J* = 1.8 Hz), 125.2 (d, *J* = 2.6 Hz), 124.9 (d, *J* = 4.5 Hz), 123.8 (d, *J* = 16.3 Hz), 120.8 (d, *J* = 5.7 Hz), 108.9 (d, *J* = 20.5 Hz), 42.4, 29.7, 22.4.

Elemental analysis: calcd (%) for $C_{17}H_{16}FNS$ (285.38): C 71.55, H 5.65; found: C 71.48, H 5.36.

Cyclopropyl(5-(pyren-1-yl)thiophen-2-yl)methanone (1o)

Following the procedure **A**, from cyclopropyl(thiophen-2-yl)methanone (0.228 g, 1.5 mmol), 1-bromopyrene (0.281 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1o** was obtained in 84% yield (0.296 g) as a white solid: mp 193-195 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.49 (d, *J* = 9.3 Hz, 1H), 8.30-8.16 (m, 3H), 8.15-8.02 (m, 5H), 7.98 (d, *J* = 3.8 Hz, 1H), 7.44 (d, *J* = 3.8 Hz, 1H), 2.70-2.61 (m, 1H), 1.40-1.32 (m, 2H), 1.16-1.07 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.9, 150.8, 145.1, 131.8, 131.7, 131.4, 130.8, 129.0, 128.9, 128.6, 128.5, 128.3, 128.1, 127.3, 126.3, 125.7, 125.4, 125.0, 124.7, 124.4, 18.0, 11.4.

Elemental analysis: calcd (%) for $C_{24}H_{16}OS$ (352.45): C 81.79, H 4.58; found: C 81.90, H 4.38.

1-(5-(Pyren-1-yl)thiophen-2-yl)ethan-1-one (1p)[19]

Following the procedure **A**, from 2-acetylthiophene (0.189 g, 1.5 mmol), 1-bromopyrene (0.281 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1p** was obtained in 79% yield (0.257 g) as a white solid mp 116-118 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.46 (d, *J* = 9.3 Hz, 1H), 8.24-8.01 (m, 8H), 7.83 (d, *J* = 3.8 Hz, 1H), 7.40 (d, *J* = 3.8 Hz, 1H), 2.68 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.8, 151.6, 144.7, 132.9, 131.8, 131.5, 130.9, 129.1, 129.0, 128.7, 128.6, 128.5, 128.2, 127.4, 126.5, 125.9, 125.5, 125.1, 124.8, 124.7, 124.4, 26.9.

Ethyl 5-(pyren-1-yl)thiophene-2-carboxylate (1q)

Following the procedure **A**, from ethyl thiophene-2-carboxylate (0.234 g, 1.5 mmol), 1-bromopyrene (0.281 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1q** was obtained in 82% yield (0.292 g) as a white solid: mp 146-148 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.47 (d, *J* = 9.3 Hz, 1H), 8.29-8.17 (m, 3H), 8.16-8.03 (m, 5H), 7.97 (d, *J* = 3.8 Hz, 1H), 7.38 (d, *J* = 3.8 Hz, 1H), 4.45 (q, *J* = 7.6 Hz, 2H), 1.46 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.3, 149.7, 134.1, 133.6, 131.6, 131.4, 130.8, 129.0, 128.6, 128.4, 128.3, 128.2, 127.3, 126.3, 125.7, 125.4, 125.0, 124.7, 124.6, 124.4, 61.3, 14.4.

Elemental analysis: calcd (%) for $C_{23}H_{16}O_2S$ (356.44): C 77.50, H 4.52; found: C 77.26, H 4.67.

2-Isobutyl-5-(pyren-1-yl)thiazole (1r)

Following the procedure **A**, from 2-isobutylthiazole (0.211 g, 1.5 mmol), 1-bromopyrene (0.281 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1r** was obtained in 91% yield (0.310 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.38 (d, *J* = 9.2 Hz, 1H), 8.15-8.09 (m, 2H), 8.07-7.94 (m, 6H), 7.93 (s, 1H), 3.05 (d, *J* = 7.6 Hz, 2H), 2.36-2.24 (m, 1H), 1.17 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.0, 141.5, 136.2, 131.3, 131.2, 130.8, 129.2, 128.4, 128.2, 128.0, 127.2, 126.2, 126.0, 125.5, 125.2, 124.9, 124.6, 124.5, 124.3, 42.6, 30.0, 22.5.

Elemental analysis: calcd (%) for $C_{23}H_{19}NS$ (341.47): C 80.90, H 5.61; found: C 81.14, H 5.39.

1-(5-(Pyren-1-yl)thiazol-2-yl)ethan-1-one (1s)

Following the procedure **A**, from 2-acetylthiazole (0.190 g, 1.5 mmol), 1-bromopyrene (0.281 g, 1 mmol) and $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), compound **1s** was obtained in 81% yield (0.265 g) as a yellow solid mp 98-100 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.35 (d, *J* = 9.2 Hz, 1H), 8.28-8.19 (m, 4H), 8.18-8.12 (m, 2H), 8.11-8.03 (m, 3H), 2.82 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.8, 166.9, 145.3, 144.1, 132.1, 131.3, 130.7, 129.2, 129.0, 128.7, 128.4, 127.2, 126.5, 126.0, 125.7, 124.9, 124.7, 124.6, 124.5, 123.8, 25.9.

Elemental analysis: calcd (%) for $C_{21}H_{13}NOS$ (327.40): C 77.04, H 4.00; found: C 76.69, H 3.68.

Procedure B (Bromination of compounds 1a-1s): To a 25 mL oven dried Schlenk tube, the arylated heteroarene derivatives **1a-1s** (1 mmol), *N*-bromosuccinimide (0.356 g, 2 mmol) and DMF (2 mL) were successively added. The reaction mixture was stirred at 25 °C for 16 hours. After concentration, the crude mixture was filtered by silica column chromatography (diethyl ether:heptane 1:4) to afford the desired brominated products which were used without further purification.

1-(5-([1,1'-Biphenyl]-2-yl)-4-bromothiophen-2-yl)ethan-1-one (2a)

Following the procedure **B**, from 1-(5-([1,1'-biphenyl]-2-yl)thiophen-2-yl)ethan-1-one **1a** (0.278, 1 mmol), compound **2a** was obtained in 86% yield (0.307 g) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.60-7.42 (m, 5H), 7.33-7.24 (m, 5H), 2.50 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 189.7, 147.3, 143.3, 142.5, 140.3, 134.9, 131.6, 130.6, 130.4, 129.9, 129.3, 128.2, 127.4, 127.3, 111.0, 26.4.

(5-([1,1'-Biphenyl]-2-yl)-4-bromothiophen-2-yl)(cyclopropyl)methanone (2b)

Following the procedure **B**, from (5-([1,1'-biphenyl]-2-yl)thiophen-2-yl)(cyclopropyl)methanone **1b** (0.307, 1 mmol), compound **2b** was obtained in 85% yield (0.325 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.62-7.42 (m, 5H), 7.30-7.20 (m, 5H), 2.46-2.35 (m, 1H), 1.26-1.19 (m, 2H), 1.06-0.99 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 192.0, 146.7, 143.7, 142.5, 140.4, 134.1, 131.7, 130.6, 130.5, 129.9, 129.3, 128.2, 127.4, 127.3, 111.1, 17.8, 11.9.

Ethyl 5-([1,1'-biphenyl]-2-yl)-4-bromothiophene-2-carboxylate (2c)

Following the procedure **B**, from ethyl 5-([1,1'-biphenyl]-2-yl)thiophene-2-carboxylate **1c** (0.308, 1 mmol), compound **2c** was obtained in 83% yield (0.321 g) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63 (s, 1H), 7.58-7.42 (m, 4H), 7.35-7.25 (m, 5H), 4.35 (q, *J* = 7.6 Hz, 2H), 1.38 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 161.2, 145.5, 142.6, 140.4, 135.6, 133.6, 131.9, 130.6, 130.4, 129.9, 129.3, 128.2, 127.4, 127.3, 111.0, 61.6, 14.4.

1-(5-([1,1'-Biphenyl]-2-yl)-4-bromo-3-chlorothiophen-2-yl)ethan-1-one (2d)

Following the procedure **B**, from 1-(5-([1,1'-biphenyl]-2-yl)-3-chlorothiophen-2-yl)ethan-1-one **1d** (0.313, 1 mmol), compound **2d** was obtained in 78% yield (0.305 g) as a white solid: mp 151-153 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.60-7.42 (m, 4H), 7.33-7.28 (m, 3H), 7.27-7.21 (m, 2H), 2.67 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 189.3, 145.8, 142.4, 140.0, 137.3, 131.4, 130.7, 130.5, 129.2, 129.0, 128.3, 127.5, 127.4, 114.4, 29.7.

Methyl 5-([1,1'-biphenyl]-2-yl)-4-bromofuran-2-carboxylate (2e)

Following the procedure **B**, from methyl 5-([1,1'-biphenyl]-2-yl)furan-2-carboxylate **1e** (0.278, 1 mmol), compound **2e** was obtained in 61% yield (0.218 g) as a white solid: mp 96-98 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.62 (d, *J* = 8.0 Hz, 1H), 7.57-7.47 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.34-7.26 (m, 3H), 7.24-7.18 (m, 2H), 7.14 (s, 1H), 3.79 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 158.2, 154.7, 143.4, 142.7, 140.6, 130.5, 130.4, 128.7, 128.2, 127.3, 127.2, 126.7, 121.7, 100.1, 52.0.

5-([1,1'-Biphenyl]-2-yl)-4-bromo-2-isobutylthiazole (2g)

Following the procedure **B**, from 5-([1,1'-biphenyl]-2-yl)-2-isobutylthiazole **1g** (0.293, 1 mmol), compound **2g** was obtained in 87% yield (0.323 g) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.59-7.40 (m, 4H), 7.33-7.21 (m, 5H), 2.76 (d, *J* = 7.6 Hz, 2H), 2.09-1.98 (m, 1H), 0.94 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.7, 142.8, 140.4, 133.8, 132.1, 131.9, 130.3, 129.4, 128.8, 128.1, 127.3, 124.9, 123.8, 42.4, 29.7, 22.2.

1-(5-([1,1'-Biphenyl]-2-yl)-4-bromothiazol-2-yl)ethan-1-one (2h)

Following the procedure **B**, from 1-(5-([1,1'biphenyl]-2-yl)thiazol-2-yl)ethan-1-one **1h** (0.279, 1 mmol), compound **2h** was obtained in 64% yield (0.229 g) as a white solid: mp 107-109 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.63-7.55 (m, 1H), 7.54-7.45 (m, 3H), 7.32-7.28 (m, 3H), 7.22-7.18 (m, 2H), 2.68 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.7, 165.4, 142.7, 142.1, 139.8, 131.5, 130.6, 130.2, 129.3, 128.3, 127.8, 127.6, 127.5, 126.7, 25.6.

1-(4-Bromo-5-(naphthalen-1-yl)thiophen-2-yl)ethan-1-one (2i)

Following the procedure **B**, from 1-(5-(naphthalen-1-yl)thiophen-2-yl)ethan-1-one **1i** (0.252, 1 mmol), compound **2i** was obtained in 48% yield in an impure form (85% purity, 0.187 g) as a yellow solid: mp 116-118 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.97 (d, *J* = 6.8 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 1H), 7.77-7.65 (m, 2H), 7.55-7.44 (m, 4H), 2.64 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.6, 149.5, 144.6, 132.6, 132.4, 132.2, 129.4, 128.8, 128.3, 127.8, 127.7, 127.6, 125.9, 124.4, 26.8.

1-(4-Bromo-5-(4-fluoronaphthalen-1-yl)thiophen-2-yl)ethan-1-one (2j)

Following the procedure **B**, from 1-(5-(4-fluoronaphthalen-1-yl)thiophen-2-yl)ethan-1-one **1j** (0.270, 1 mmol), compound **2j** was obtained in 65% yield (0.226 g) as a white solid: mp 92-94 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.19 (d, *J* = 7.8 Hz, 1H), 7.75 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.65-7.57 (m, 2H), 7.48 (dd, *J* = 7.9, 5.3 Hz, 1H), 7.24 (dd, *J* = 10.0, 8.0 Hz, 1H), 2.61 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 189.7, 159.8 (d, *J* = 255.7 Hz), 144.6, 143.7, 135.0, 132.8 (d, *J* = 5.2 Hz), 129.2 (d, *J* = 8.9 Hz), 127.9, 126.7 (d, *J* = 1.9 Hz), 125.7 (d, *J* = 2.6 Hz), 125.4 (d, *J* = 4.5 Hz), 123.8 (d, *J* = 16.5 Hz), 121.1 (d, *J* = 5.6 Hz), 112.0, 109.0 (d, *J* = 20.6 Hz), 26.5.

(4-Bromo-5-(naphthalen-1-yl)thiophen-2-yl)(cyclopropyl)methanone (2k)

Following the procedure **B**, from cyclopropyl(5-(naphthalen-1-yl)thiophen-2-yl)methanone **1k** (0.278, 1 mmol), compound **2k** was obtained in 45% yield as a colorless oil in an impure form (60% purity, 0.269 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.00-7.65 (m, 4H), 7.58-7.47 (m, 4H), 2.64-2.51 (m, 1H), 1.38-1.30 (m, 2H), 1.14-1.05 (m, 2H).

Ethyl 4-bromo-5-(naphthalen-1-yl)thiophene-2-carboxylate (2l)

Following the procedure **B**, from ethyl 5-(naphthalen-1-yl)thiophene-2-carboxylate **1l** (0.282, 1 mmol), compound **2l** was obtained in 49% yield as a colorless oil in an impure form (75% purity, 0.236 g).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.97 (d, *J* = 6.8 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 1H), 7.85-7.73 (m, 2H), 7.57-7.47 (m, 4H), 4.46 (q, *J* = 7.6 Hz, 2H), 1.47 (t, *J* = 7.6 Hz, 3H).

4-Bromo-2-isobutyl-5-(naphthalen-1-yl)thiazole (2m)

Following the procedure **B**, from 2-isobutyl-5-(naphthalen-1-yl)thiazole **1m** (0.267, 1 mmol), compound **2m** was obtained in 63% yield (0.218 g) as a white solid: mp 128-130 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.00-7.91 (m, 2H), 7.83-7.76 (m, 1H), 7.60-7.50 (m, 4H), 2.97 (d, *J* = 7.6 Hz, 2H), 2.31-2.17 (m, 1H), 1.12 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.1, 133.7, 132.0, 130.2, 129.9, 129.7, 128.5, 127.6, 126.9, 126.3, 125.6, 125.2, 124.5, 42.7, 29.8, 22.4.

4-Bromo-5-(4-fluoronaphthalen-1-yl)-2-isobutylthiazole (2n)

Following the procedure **B**, from 5-(4-fluoronaphthalen-1-yl)-2-isobutylthiazole **1n** (0.285, 1 mmol), compound **2n** was obtained in 68% yield (0.247 g) as a white solid: mp 99-101 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.18 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.62-7.53 (m, 2H), 7.47 (dd, *J* = 7.9, 5.3 Hz, 1H), 7.20 (dd, *J* = 10.0, 8.0 Hz, 1H), 2.93 (d, *J* = 7.6 Hz, 2H), 2.26-2.24 (m, 1H), 1.07 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.2, 159.5 (d, *J* = 255.3 Hz), 133.4 (d, *J* = 5.2 Hz), 129.6 (d, *J* = 8.9 Hz), 129.4, 127.8, 126.6 (d, *J* = 1.8 Hz), 125.6 (d, *J* = 2.5 Hz), 124.8, 123.9 (d, *J* = 16.5 Hz), 123.5 (d, *J* = 4.5 Hz), 121.0 (d, *J* = 5.5 Hz), 109.1 (d, *J* = 20.6 Hz), 42.7, 29.8, 22.4.

Procedure C (Direct intramolecular arylation of heteroarenes): To a 25 mL oven dried Schlenk tube, heteroaryl bromide (0.5 mmol), KOPiv (0.140 g, 1 mmol), DMA (2 mL) and $PdCl(C_3H_5)$(dppb) (6.1 mg, 0.01 mmol) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 150 °C (oil bath temperature) for 3 or 16 hours (see scheme 5). After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography (diethyl ether:heptane 2:3) to afford the desired products.

1-(Phenanthro[9,10-*b*]thiophen-2-yl)ethan-1-one (3a)

Following the procedure **C**, from 1-(5-([1,1'-biphenyl]-2-yl)-4-bromothiophen-2-yl)ethan-1-one **2a** (0.179 g, 0.5 mmol), compound **3a** was obtained in 87% yield (0.120 g) as a yellow solid: mp 218-220 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.70-8.62 (m, 2H), 8.47 (s, 1H), 8.31-8.25 (m, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.76-7.61 (m, 4H), 2.75 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 191.4, 142.4, 142.2, 134.9, 129.9, 129.2, 128.6, 128.2, 128.1, 127.6 (m), 127.5, 126.7, 124.9, 123.9, 123.7, 123.6, 26.9.

Elemental analysis: calcd (%) for $C_{18}H_{12}OS$ (276.35): C 78.23, H 4.38; found: C 78.39, H 4.57.

Cyclopropyl(phenanthro[9,10-*b*]thiophen-2-yl)methanone (3b)

Following the procedure **C**, from (5-([1,1'-biphenyl]-2-yl)-4-bromothiophen-2-yl)(cyclopropyl)methanone **2b** (0.192 g, 0.5 mmol), compound **3b** was obtained in 85% yield (0.128 g) as a yellow solid: mp 247-249 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.68-8.60 (m, 3H), 8.31 (d, *J* = 6.4 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.70-7.62 (m, 4H), 2.81-2.72 (m, 1H), 1.40-1.30 (m, 2H), 1.20-1.10 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.5, 142.9, 141.8, 135.0, 129.8, 129.2, 128.8, 128.0, 127.7, 127.6, 127.5, 127.2, 126.7, 124.8, 124.0, 123.7, 123.6, 18.2, 11.8.

Elemental analysis: calcd (%) for $C_{20}H_{14}OS$ (302.39): C 79.44, H 4.67; found: C 79.32, H 4.79.

Ethyl phenanthro[9,10-*b*]thiophene-2-carboxylate (3c)

Following the procedure **C**, from ethyl 5-([1,1'-biphenyl]-2-yl)-4-bromothiophene-2-carboxylate **2c** (0.193 g, 0.5 mmol), compound **3c** was obtained in 84% yield (0.128 g) as a white solid: mp 190-192 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.67 (d, *J* = 8.6 Hz, 2H), 8.64 (s, 1H), 8.34-8.30 (m, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.74-7.61 (m, 4H), 4.49 (q, *J* = 7.6 Hz, 2H), 1.50 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.7, 141.1, 134.7, 132.2, 129.7, 129.2, 129.1, 128.6, 127.8, 127.7, 127.5, 126.6, 124.6, 124.2, 123.7, 123.5, 61.6, 14.4.

Elemental analysis: calcd (%) for $C_{19}H_{14}O_2S$ (306.38): C 74.49, H 4.61; found: C 74.67, H 4.90.

Methyl phenanthro[9,10-*b*]furan-2-carboxylate (3e)

Following the procedure **C**, from methyl 5-([1,1'-biphenyl]-2-yl)-4-bromofuran-2-carboxylate **2e** (0.178 g, 0.5 mmol), compound **3e** was obtained in 84% yield (0.116 g) as a white solid: mp 156-158 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.62 (d, *J* = 6.4 Hz, 2H), 8.44-8.40 (m, 1H), 8.06 (d, *J* = 7.0 Hz, 1H), 7.93 (s, 1H), 7.69-7.59 (m, 4H), 4.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.7, 151.3, 144.6, 130.6, 128.4, 127.5, 127.4, 127.3, 126.8, 126.0, 123.9, 123.6, 123.4, 121.8, 121.6, 120.5, 113.7, 52.2.

Elemental analysis: calcd (%) for $C_{18}H_{12}O_3$ (276.29): C 78.25, H 4.38; found: C 78.39, H 4.61.

2-Isobutylphenanthro[9,10-*d*]thiazole (3g)

Following the procedure **C**, from 5-([1,1'-biphenyl]-2-yl)-4-bromo-2-isobutylthiazole **2g** (0.186 g, 0.5 mmol), compound **3g** was obtained in 90% yield (0.131 g) as a yellow solid: mp 118-120 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.93 (d, *J* = 7.6 Hz, 1H), 8.62-8.55 (m, 2H), 7.88-7.84 (m, 1H), 7.77 (t, *J* = 7.2 Hz, 1H),7.67 (t, *J* = 7.6 Hz, 1H), 7.58-7.54 (m, 2H), 3.12 (d, *J* = 7.6 Hz, 2H), 2.45-2.30 (m, 1H), 1.17 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.5, 148.6, 130.5, 129.7, 128.7, 128.2, 127.3 (m), 127.2, 126.6, 126.3, 125.8, 124.9, 123.6, 123.0, 43.2, 30.0, 22.6.

Elemental analysis: calcd (%) for $C_{19}H_{17}NS$ (291.41): C 78.31, H 5.88; found: C 78.61, H 5.74.

1-(Acenaphtho[1,2-*b*]thiophen-8-yl)ethan-1-one (4i)[20]

Following the procedure **C**, from 1-(4-bromo-5-(naphthalen-1-yl)thiophen-2-yl)ethan-1-one **2i** (0.166 g, 0.5 mmol), compound **4i** was obtained in 53% yield (0.066 g) as a yellow solid: mp 149-151 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.96 (s, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.84 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 6.9 Hz, 1H), 7.63-7.57 (m, 2H), 2.65 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 190.9, 149.0, 146.9, 145.3, 134.0, 132.9, 132.4, 129.6, 128.3, 127.9 (m), 126.7, 125.0, 122.3, 121.2, 26.7.

Acenaphtho[1,2-*b*]thiophen-8-yl(cyclopropyl)methanone (4k)

Following the procedure **C**, from (4-bromo-5-(naphthalen-1-yl)thiophen-2-yl)(cyclopropyl)methanone **2k** (0.179 g, 0.5 mmol), compound **4k** was obtained in 51% yield (0.070 g) as a yellow solid: mp 99-101 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.07 (s, 1H), 7.88-7.75 (m, 3H), 7.73 (d, *J* = 6.9 Hz, 1H), 7.61-7.55 (m, 2H), 2.66-2.55 (m, 1H), 1.38-1.29 (m, 2H), 1.14-1.05 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 193.1, 148.5, 147.5, 134.0, 133.0, 132.5, 129.5, 128.2, 127.9 (m), 126.7, 124.1, 122.2, 121.1, 18.0, 11.4.

Elemental analysis: calcd (%) for $C_{18}H_{12}OS$ (276.35): C 78.23, H 4.38; found: C 77.98, H 4.25.

Ethyl acenaphtho[1,2-*b*]thiophene-8-carboxylate (4l)[20]

Following the procedure **C**, from ethyl 4-bromo-5-(naphthalen-1-yl)thiophene-2-carboxylate **2l** (0.181 g, 0.5 mmol), compound **4l** was obtained in 38% yield (0.053 g) as a yellow solid: mp 178-180 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.12 (s, 1H), 7.90-7.76 (m, 4H), 7.64-7.58 (m, 2H), 4.44 (q, *J* = 7.6 Hz, 2H), 1.46 (t, *J* = 7.6 Hz, 3H).

8-Isobutylacenaphtho[1,2-*d*]thiazole (4m)

Following the procedure **C**, from 4-bromo-2-isobutyl-5-(naphthalen-1-yl)thiazole **2m** (0.173 g, 0.5 mmol), compound **4m** was obtained in 21% yield (0.028 g) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.02 (d, *J* = 6.9 Hz, 1H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 6.9 Hz, 1H), 7.61 (t, *J* = 8.1 Hz, 1H), 7.57 (t, *J* = 8.1 Hz, 1H), 3.04 (d, *J* = 7.6 Hz, 2H), 2.33-2.17 (m, 1H), 1.10 (d, *J* = 7.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 173.6, 160.4, 133.6, 131.9, 131.8, 130.9, 129.2, 127.8, 127.6, 127.3, 127.2, 121.8, 121.4, 43.4, 30.1, 22.4.

Elemental analysis: calcd (%) for $C_{17}H_{15}NS$ (265.37): C 76.94, H 5.70; found: C 77.20, H 5.60.

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