

Synthesis of Symmetrical and Unsymmetrical 1,3-Diheteroarylbenzenes Through Palladium-Catalyzed Direct Arylation of Benzene-1,3-disulfonyl Dichloride and 3-Bromobenzenesulfonyl Chlorides

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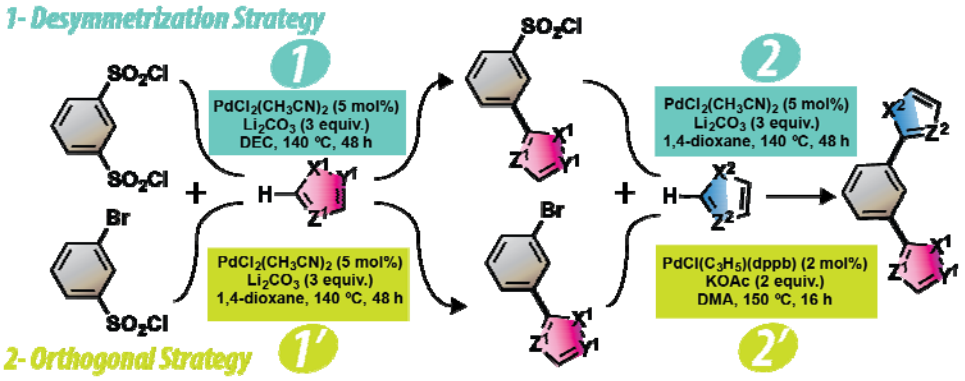
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Graphical Abstract

Synthesis of Symmetrical and Unsymmetrical 1,3-Diheteroarylbenzenes Through Palladium-Catalyzed Direct Arylation of Benzene-1,3-disulfonyl Dichloride and 3-Bromobenzenesulfonyl Chlorides

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Imane Idris,[a, b] Fazia Derridj, [a, b, c] Safia Djebbar,[c] Jean-François Soulé, [a,] * and Henri Doucet [a,] *

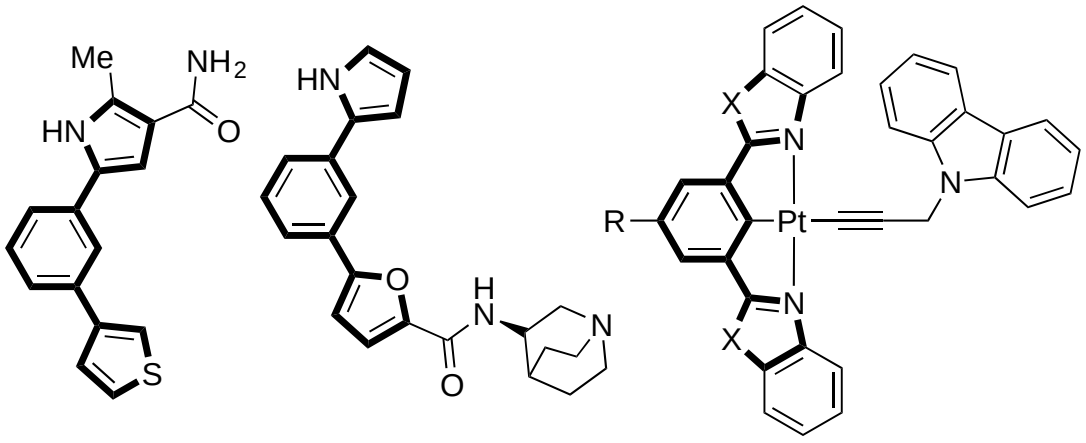
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ABSTRACT

The palladium-catalyzed synthesis of unsymmetrical 1,3-diheteroarylbenzenes was investigated. The first synthetic pathway relies on the desymmetrization of benzene-1,3-disulfonyl dichloride through two successive palladium-catalyzed direct desulfitative arylations with two different heteroarenes. The second strategy employs the orthogonal functionalization of 3-bromobenzenesulfonylchloride using an iterative C–H bond arylation sequence, namely, palladium-catalyzed direct desulfitative arylation followed by a palladium-catalyzed direct arylation step using aryl bromide as the coupling partner. The synthesis of symmetrical 1,3-diheteroarylbenzenes was also investigated.

Keywords:
C–H Arylation, Catalysis, Desulfitative, Tridentate Ligand, Palladium

1. Introduction



I **II** **III**

Figure 1. Examples of uses of 1,3-diheteroarylbenzenes.

1,3-Diheteroarylbenzenes are an important class of molecules in organic chemistry. Unsymmetrical 1,3-diheteroarylbenzenes, such as molecule **I,** which contains 3-thienyl and 2-pyrrolyl substituents, are useful agents in the treatment of diseases, including inflammatory diseases, cancer, and AIDS (Figure 1).[1] *N*-Quinuclidinyl-heteroaryl amide **II,** which contains both 2-furyl and 2-pyrrolyl moieties, has shown potential pharmaceutical uses in the

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treatment of neurological disorders (Figure 1).[2] Moreover, they are ubiquitous subunits embedded in number of tridentate ligands such as N^C^N, which found many applications in electronic devices or in catalysis.[3]

For example, the family of complexes **III,** based on 1,3-bis-heteroazolylbenzenes ligand, displays tunable color luminescent properties, which has plenty of applications in the construction of organic light-emitting (OLED) devices (Figure 1).[4] 1,3-Diheteroarylbenzenes are generally synthesized from isophthalaldehydes *via* a double condensation with 2-aminophenols or 2-aminobenzenethiols (Figure 2A).[5] However, this methodology is limited to the synthesis of symmetrical compounds. A few examples of preparation of unsymmetrical 1,3-diheteroarylbenzenes have been reported starting from 3-bromobenzaldehydes *via* a condensation of the aldehyde function with amines followed by palladium-catalyzed C–C bond formation (e.g., Negishi or Suzuki reactions) (Figure 2B).[6] An other synthetic pathway involved double palladium-catalyzed C–C bond formation using 1,3-dibromobenzene and organometallic reagents (Figure 2C).[7] This methodology is limited to the synthesis of symmetrical compounds, albeit some reports focused on the desymmetrization of 1,3-dibromobenzene using selective mono-coupling based on Suzuki reaction.[8] Dodd and co-workers reported the synthesis of unsymmetrical 1,3-diheteroarylbenzenes using an one-pot procedure involving double Suzuki reaction with two different boronic acids.[9] Since these last decades, palladium–catalyzed direct arylation has emerged as one of the most eco-friendly methods for the fast synthesis of complex molecules.[10] Thanks to this methodology, we recently synthesized symmetrical 1,3-diheteroarylbenzenes from 1,3-dibromobenzenes (Figure 2C).[11] However, this synthetic pathway does not allow the synthesis of unsymmetrical compounds due to the very high reactivity of 1,3-dibromobenzenes. Recently, based on the pioneering works reported by Dong and co-workers,[12] our group and others have exploited the reactivity of benzenesulfonyl chlorides for direct regioselective arylation of several heteroarenes.[13] Similar desulfitative direct arylations were also reported using of sodium arylsulfinates,[14] and arylsulfonyl hydrazides.[15] It generally displays high reactivities and regioselectivities with good tolerances to C–X bonds.[16] In addition, the β-regioselectivity for the arylation of (benzo)thiophenes is an important advantage compared to other arylating agents.[17] In the course of our investigations, we found that the desulfitative C–H bond arylations were highly dependent to the benzenesulfonyl chloride electronic properties. As electron-poor benzenesulfonyl chlorides react faster than electron-rich ones, we assumed that with such reactants it should be possible to desymmetrize benzene-1,3-disulfonyl dichloride to allow the synthesis of unsymmetrical 1,3-diheteroarylbenzenes. Indeed, sulfonyl chloride has an electron-withdrawing character in contrast to heteroarenes which have electron-donating characters; hence the first desulfitative arylation should be faster than the second one. (Figure 2D). Moreover, thanks to the orthogonal reactivity of desulfitative C–H bond arylations, which tolerates C–Br bonds, we proposed a new synthetic approach to the construction of unsymmetrical 1,3-diheteroarylbenzenes from 3-bromobenzenesulfonyl chlorides through iterative direct arylations (Figure 1E).

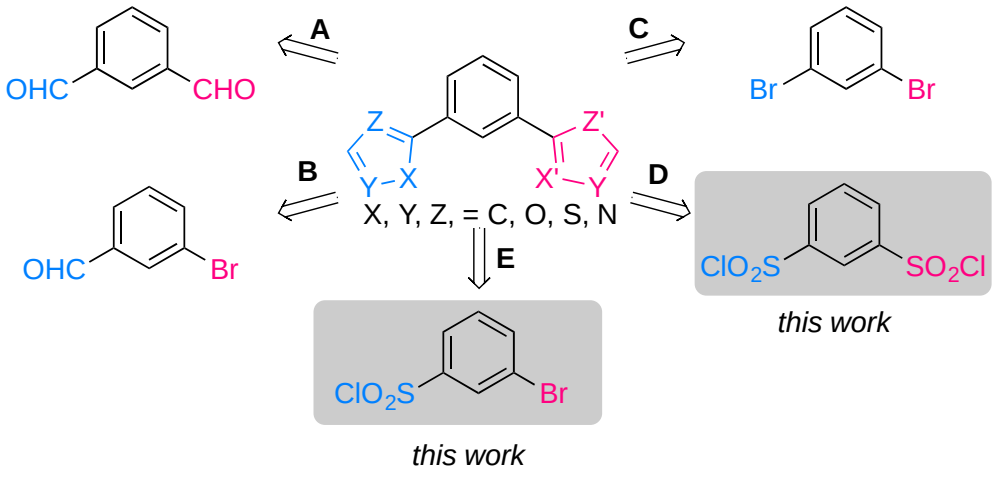


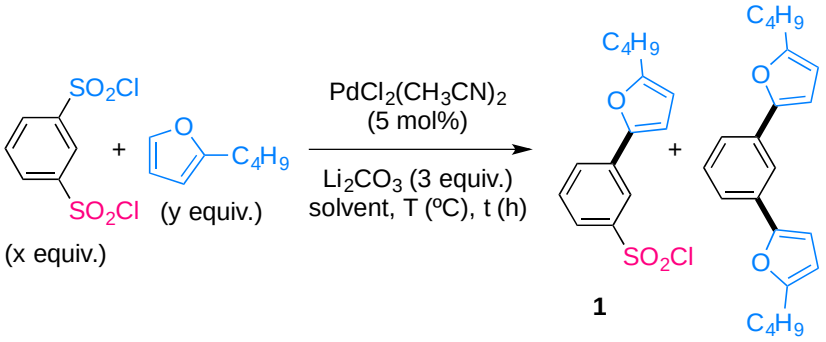
Figure 2. Retrosynthetic pathways of 1,3-diheteroarylbenzenes.

2. Results and Discussion.

We started our investigation by studying the reactivity of benzene-1,3-disulfonyl dichloride as arylating source for the C–H bond arylation of 2-*n*-butylfuran (Table 1). First, we attempted to prepare the monoarylated product **1** using our previous optimized reaction conditions for the C–H bond arylation of furans,[13d] (i.e., 5 mol% of $PdCl_2(CH_3CN)_2$ in the presence of Li_2CO_3 as base in 1,4-dioxane at 140 ºC during 48 h) with a slight excess amount of benzene-1,3-disulfonyl dichloride (1.5 equiv.). As result, we obtained a mixture of monoarylated and diarylated products **1** and **2** in 45:55 ratio (Table 1, entry 1). To improve the yield in **1**, both the solvent influence and the temperature were screened. We had previously demonstrated that the reaction could also be performed in green solvents such as diethyl carbonate (DEC) or cyclopentylmethyl ether (CPME) with comparable yields but with a lower reaction rates.[18] When the reaction was performed in DEC, the monoarylation product **1** was obtained in 95% selectivity with a full conversion of 2-*n*-butylfuran (Table 1, entry 2). A lower selectivity and reactivity was observed using CPME as solvent (87% of **1**) (Table 1, entry 3). The use of 1,4-dioxane at only 110 ºC and a shorter reaction time (18 h)

also furnished a high selectivity in favor of the monoarylated product **1** (Table 1, entry 4). No reaction occurred using polar and protic solvent such as DMF or butan-1-ol (Table 1, entries 5 and 6). Using these two optimized reaction conditions, i.e., DEC at 140 ºC during 48 h and 1,4-dioxane at 110 ºC during 18 h, we achieved the synthesis of **1** in very high yield (85-87%)[19] using only 1.2 equivalents of benzene-1,3-disulfonyl dichloride (Table 1, entries 7 and 8). It is important to note that the use of a lower amount of benzene-1,3-disulfonyl dichloride (1.1 equiv.) gave a slightly lower **1**:**2** ratio (Table 1, entry 9). On the other hand, the diarylated product **2** has also been synthesized in high yield using 3 equivalents of 2-*n*-butylfuran and 6 equivalents of base in 1,4-dioxane as solvent at 140 ºC during 48 h (Table 1, entry 10).

Table 1. Effect of the reaction conditions on Pd-catalyzed desulfitative coupling of benzene-1,3-disulfonyl dichloride with 2-*n*-butylfuran.

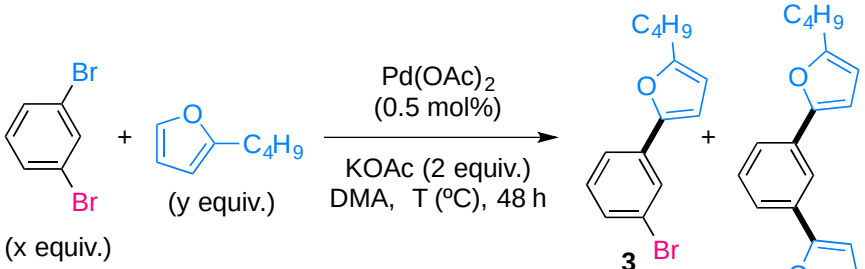


Entry	x:y	solvent	T (ºC)	t (h)	Conv. (%)[a]	**1** : **2** [b]
1	1.5:1	1,4-dioxane	140	48	100	45:55 (34% of **1**)[a, b]
2	1.5:1	DEC	140	48	100	95:5 (83% of **1**)[a, b]
3	1.5:1	CPME	140	48	72	87:13 (77%)of **1**)[a, b]
4	1.5:1	1,4-dioxane	110	18	100	95:5 (85% of **1**)[a]
5	1.5:1	DMF	110	48	0	
6	1.5:1	BuOH	140	48	0	
7	1.2:1	DEC	140	48	100	95:5 (87% of **1**)[a]
8	1.2:1	1,4-dioxane	110	48	100	94:6 (85% of **1**)[a]
9	1.1:1	1,4-dioxane	140	48	100	90:10 (76% of **1**)[a]
10[c]	1:3	1,4-dioxane	140	48	100	9:91 (84% of **2**)[d]

[a] Based on 2-*n*-butylfuran; [b] Determined using GC-MS and ^{1}H- NMR analyses, [c] 6 equiv. of Li_2CO_3 were used. [d] based on benzene-1,3-disulfonyl dichloride

Next, we performed similar experiments with 1,3-dibromobenzene as the aryl source using 0.5 mol% of $Pd(OAc)_2$ in the presence of KOAc as base in DMA at 150 ºC (Table 2). As seen previously,[11a, 11b] this substrate is very reactive and **2** was obtained as the major product, except in the presence of a huge amount (5 equiv.) of 1,3-dibromobenzene (Table 2, entries 1-3). However, the monoarylated product **3** was isolated only 52% yield. No reaction occurred at lower temperature (110 ºC), and the use of DEC as solvent had almost no effect on the **3**:**2** selectivity (Table 2, entries 4 and 5).

Table 2. Effect of the reaction conditions on Pd-catalyzed direct coupling 1,3-dibromobenzene with 2-*n*-butylfuran.

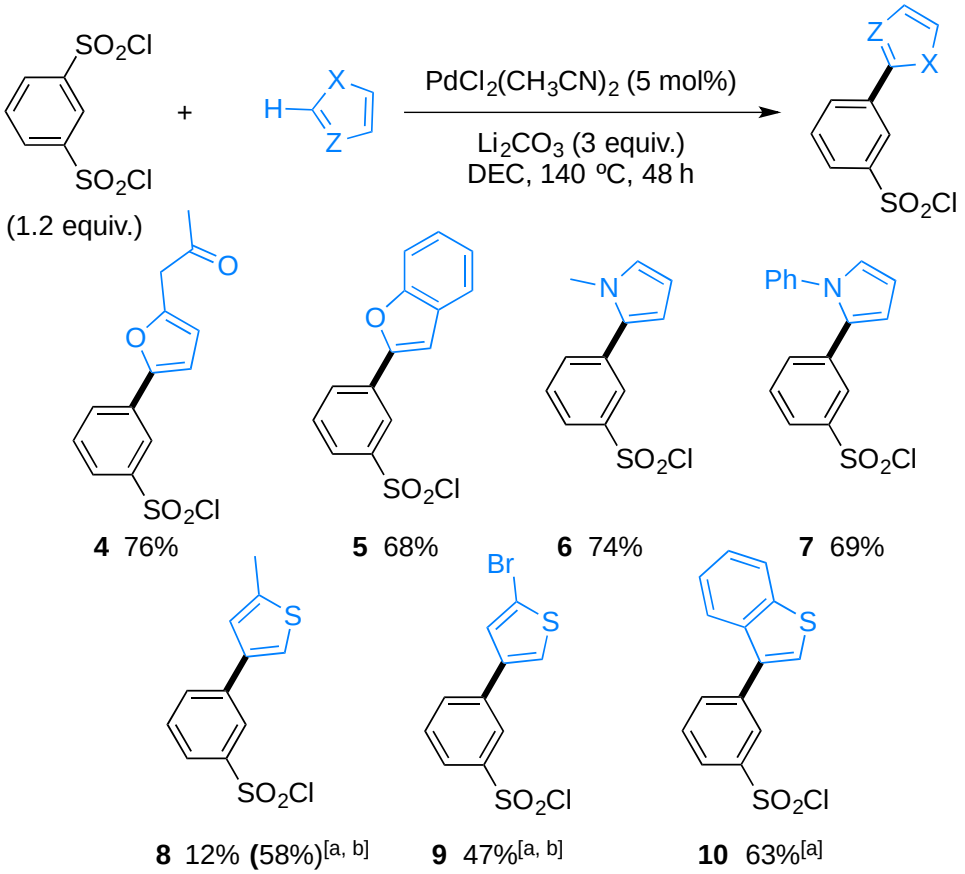


Entry	x:y	T (ºC)	Conv. (%)[a]	**3** : **2**[b]
1	1.5:1	150	100	21:79 (62% of **2**)[a, b]
2	2:1	150	100	41:59 (47% of **2**)[a, b]
3	5:1	150	100	77:33 (52% of **3**)[a]
4	5:1	110	0	–
5[c]	5:1	150	100	36:64 (52% of **2**)[a, b]

[a] Based on 2-*n*-butylfuran; [b] ratio determined using GC-MS and ^{1}H-NMR analyses; [c] DEC was used as solvent.

In contrast to 1,3-dibromobenzene, we demonstrated that benzenedisulfonyl chloride could be easily desymmetrized and consequently it represents a suitable precursor of unsymmetrical 1,3-diheteroarylbenzenes. Then, we investigated the scope of the direct desulfitative monoarylation of benzene-1,3-disulfonyl dichloride with various heteroarenes in DEC at 140 ºC (Scheme 1). 2-Furyl-2-propanone, which contains an enolizable ketone, was monoarylated to give **4** in 76% yield without any side reaction. The C2-regioselective direct arylation of benzofuran is challenging with other arylating partners.[13e] From benzene-1,3-disulfonyl dichloride, 3-(benzofuran-2-yl)benzenesulfonyl chloride (**5**) was isolated in 68% yield. *N*-protected pyrroles were also suitable heteroarenes for the mono-desulfitative arylation, as **6** and **7** were obtained in 74% and 69% yields, respectively from 1-methylpyrrole and 1-phenylpyrrole. Thiophene derivatives displayed a β-regioselectivity but with a lower reactivity in such desulfitative coupling. To overcome this poor reactivity, we performed the reaction in 1,4-dioxane at 140 ºC during 18 h. Under these conditions, we were pleased to find that the reaction occurred, and from 2-methythiophene and 2-bromothiophene the monoarylated products **8** and **9** were obtained in 58% and 47% yields, respectively, without formation of diarylated products. Benzothiophene has also been used as heteroarene for the monodesulfitative arylation of benzene-1,3-disulfonyl dichloride to afford **10** in moderate yield.

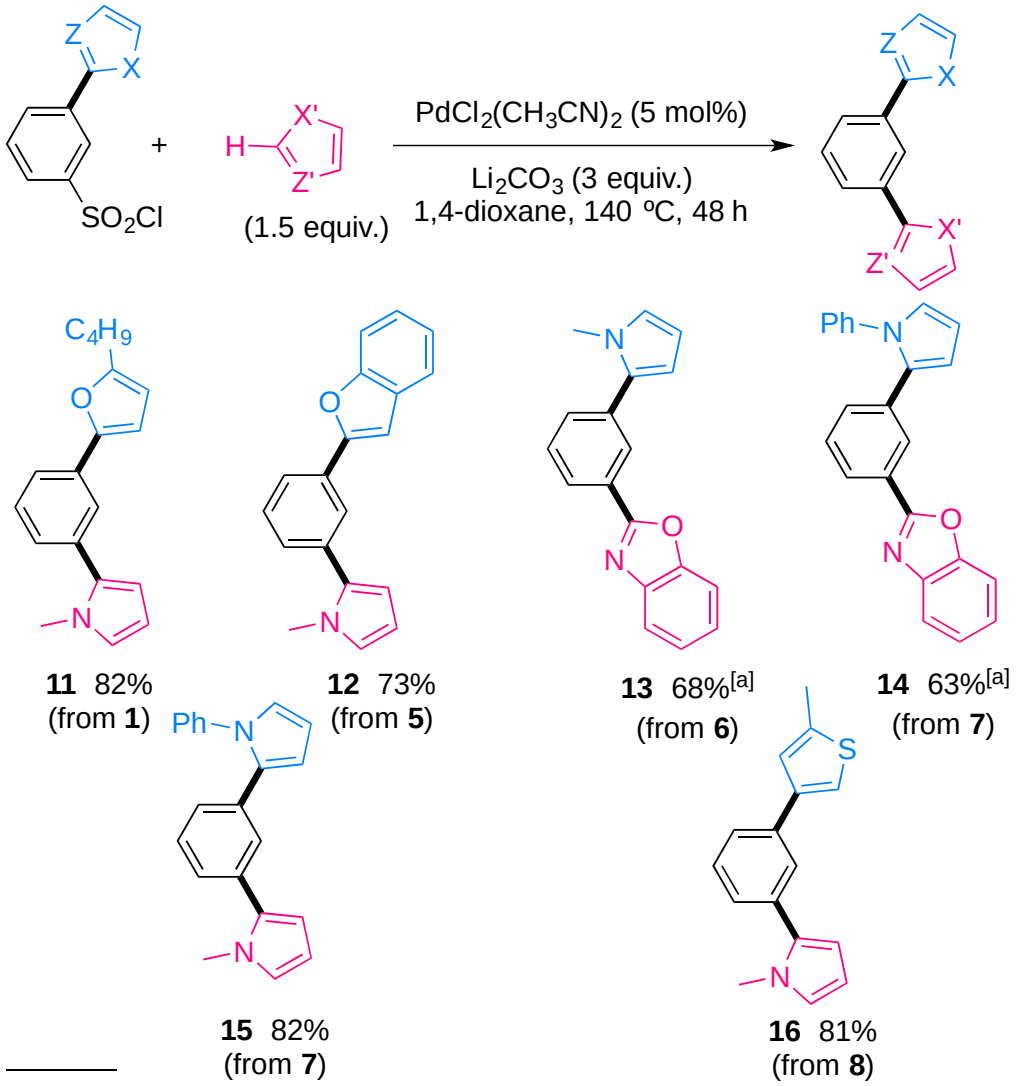
Scheme 1. Scope of the Pd-catalyzed direct desulfitative monoarylation of benzene-1,3-disulfonyl dichloride



[a] reaction was performed in 1,4-dioxane. [b] 18 h.

As for all these selective monoarylations of benzene-1,3-disulfonyl dichloride, the second benzenesulfonyl chloride function remained untouched, we investigated the reactivity of **1**, **5-8** in a second desulfitative direct arylation for the synthesis of unsymmetrical 1,3-diheteroarylbenzenes (Scheme 2). The synthesis of the unsymmetrical 1,3-diheteroarylbenzene **11** was achieved in 82% yield from **1** and 1.5 equivalents of 1-methylpyrrole using the classical reaction conditions for desulfitative direct arylation, namely, 5 mol% of $PdCl_2(CH_3CN)_2$ in the presence of Li_2CO_3 as base in 1,4-dioxane at 140 ºC during 48 h. Using the same reaction conditions, the 3-heteroarylbenzenesufonyl chloride **5** was converted into **12** in 73% yield. Then, a benzoxazole moiety was introduced on **6** and **7** to afford the desired compounds **13** and **14** in 68% and 63% yields, respectively. For these couplings, similar conditions to those reported by Cheng for the direct arylation of benzoxazole[13a] –namely, the addition of a stoichiometric amount of copper to the reaction mixture– were used. Using this methodology, the benzene **15** bearing by two different pyrrole units (1-methyl- and 1-phenylpyrroles) was obtained in high yield. This approach also allowed the synthesis of a benzene *meta* disubstituted by thiophene and pyrrole units **16** in 81% yield.

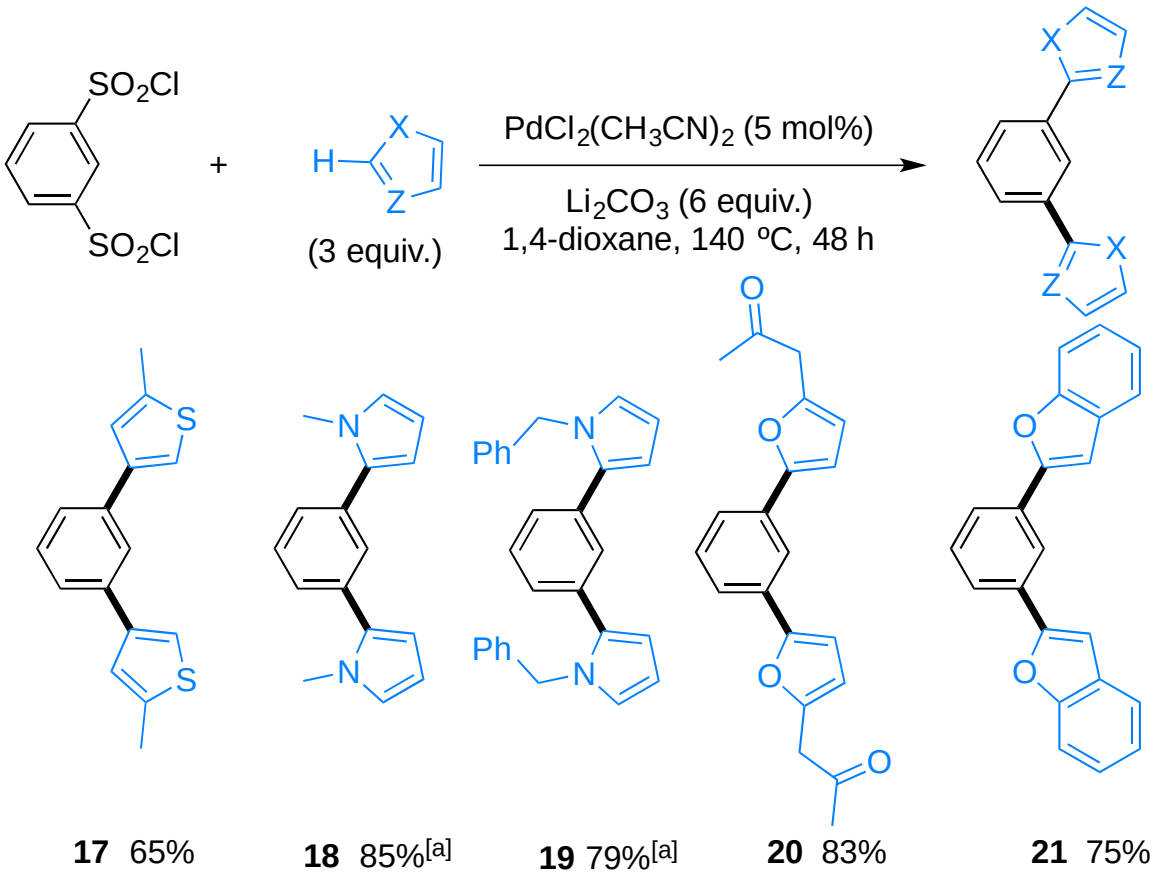
Scheme 2. Scope of the second desulfitative direct arylations: syntheses of unsymmetrical 1,3-diheteroarylbenzenes.



[a] CuI (1 equiv.) was used as additive.

Having successfully achieved the synthesis of unsymmetrical 1,3-diheteroarylbenzenes through two successive C–H bond desulfitative arylations from benzene-1,3-disulfonyl dichloride, we turned our attention to the one-pot synthesis of symmetrical 1,3-diheteroarylbenzenes (Scheme 3). Using the optimized reaction conditions for the diarylation (Table 1, entry 8), the symmetrical compounds **17-21** were isolated in high yields. Notably, a larger excess of heteroarene was required in the case of 1-methylpyrrole in order to prevent the 2,5-diarylation of the pyrrole unit. *N*-benzylpyrrole was also tolerated affording **19** in 79% yield.

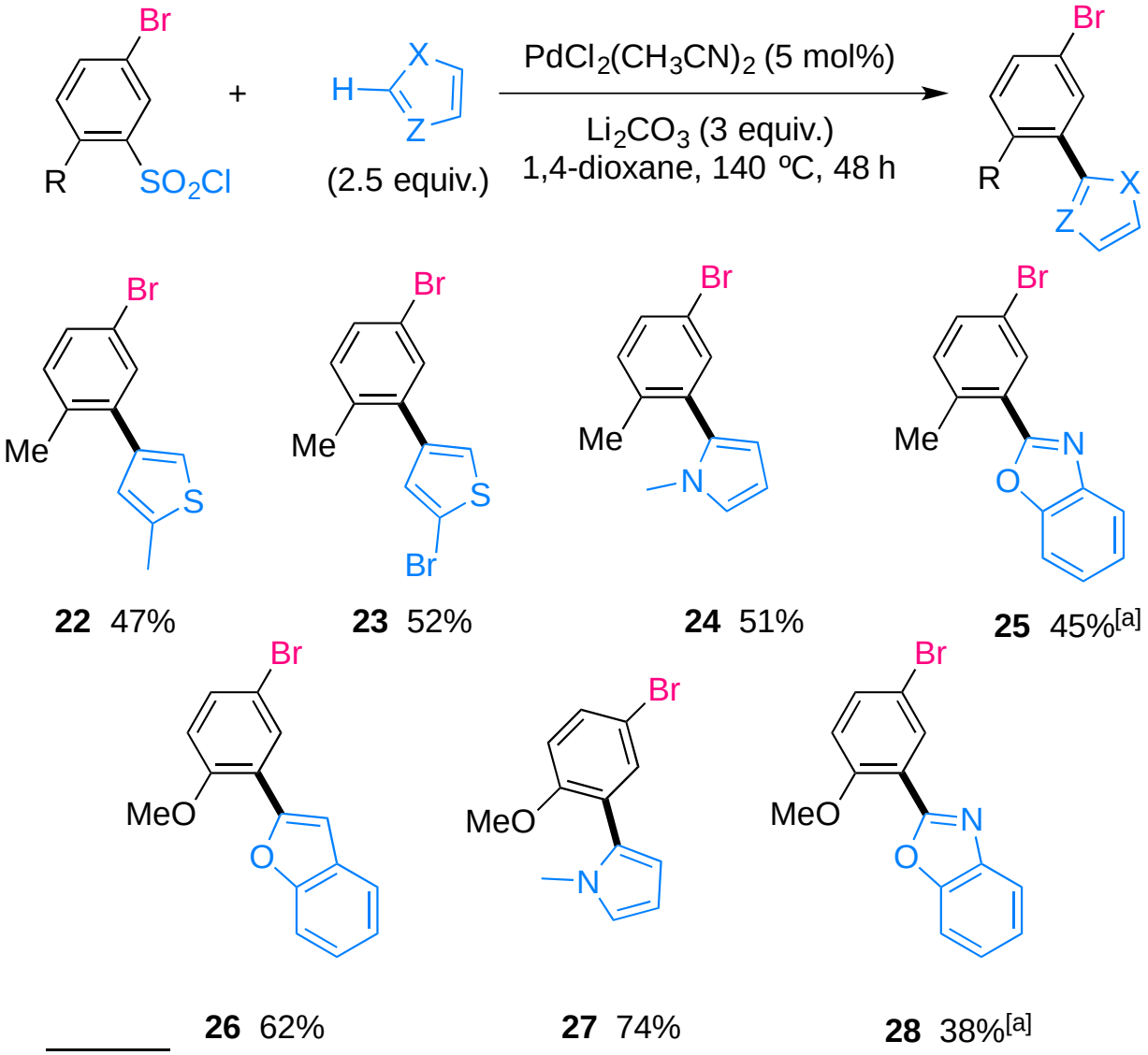
Scheme 3. Scope of the one-pot Pd-catalyzed direct desulfitative diarylation of benzene-1,3-disulfonyl dichloride.



[a] 5 equiv. of 1-methylpyrrole was used.

On the other hand, we had previously shown that palladium-catalyzed direct desulfitative arylation of heteroarenes was very chemoselective and we also demonstrated that the C–Br bonds are not involved in the catalytic cycle, allowing orthogonal functionalizations.[16] Here, we used the benefit of this unique chemoselectivity for the construction of unsymmetrical 1,3-diheteroarylbenzenes from 5-bromo-2-substituted benzenesulfonyl chlorides *via* two successive direct arylations (*i.e.*, direct desulfitative arylation followed by direct arylation of the C–Br bond) (Schemes 4 and 5). In a first step, we synthesized a set of 1-bromo-3-heteroarylbenzenes using the previous optimized conditions. In all case, no cleavage of the C–Br bond was observed. The reaction between 2-methylthiophene or 2-bromothiophene with 5-bromo-2-methylbenzenesulfonyl gave the challenging C3-arylated thiophenes **22** and **23** in 47% and 52% yields, respectively. 1-Methylpyrrole was arylated at C2-position in 51% yield. Using 1 equivalent of CuI as additive, the benzoxazole **24**, in which the arylation occurred at C1 position, was isolated in 45% yield. A similar reactivity was observed using 5-bromo-2-methoxybenzenesulfonyl chloride as aryl source allowing the formation of the 1-bromo-3-heteroarylbenzene derivatives **26**-**28** in good yields.

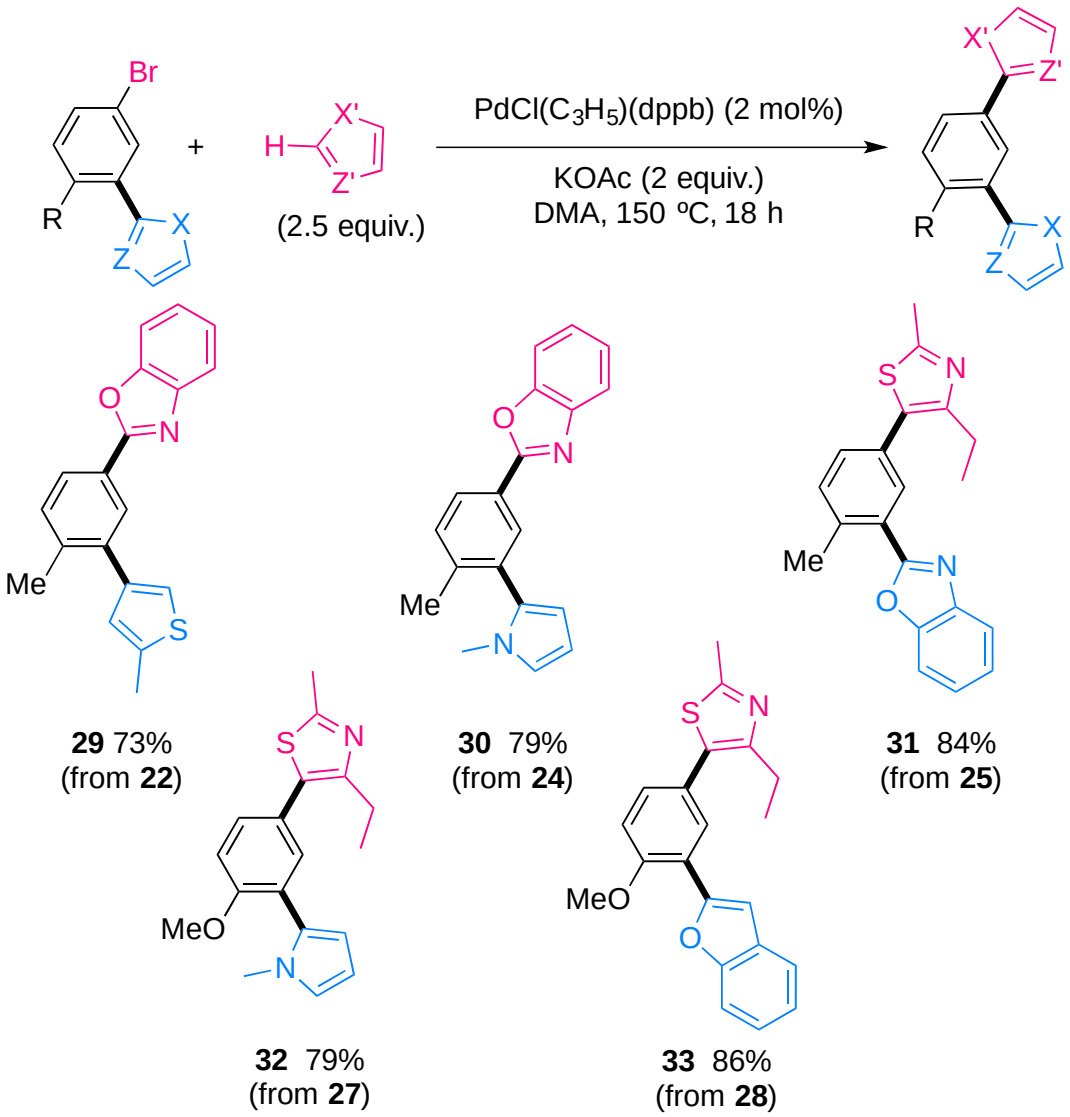
Scheme 4. Scope of the Pd-catalyzed desulfitative direct arylation with 5-bromo-2-methylbenzenesulfonyl chloride and 5-bromo-2-methoxybenzenesulfonyl chloride.



[a] CuI (1 equiv.) was used as additive

After having performed the first desulfitative C–H bond arylation, which gave 1-bromo-3-heteroarylbenzene derivatives **22-28**, a second direct arylation was performed to deliver the targeted unsymmetrical 1,3-disubstituted benzenes (Scheme 5). We selected our previous reaction conditions,[20] which have already demonstrated to be efficient for the direct arylation of heteroarenes with aryl bromides as coupling partners, i.e., 2 mol% $PdCl(C_3H_5)$(dppb) catalyst [dppb = 1,4-bis(diphenylphosphino)butane] in the presence of KOAc as base in dimethylacetamide (DMA) at 150 ºC during 16 h. When the direct arylation was performed with **22** or **24** as aryl bromide partners and benzoxazole, the desired 1,3-diheteroarylbenzenes **29** and **30** were obtained in excellent yields. We did not observe any homocoupling reaction, although the compounds **22** and **24** contain reactive C–H bonds on the thienyl or pyrrolyl units. However, from the aryl bromide **23**, which contains two different C–Br bonds, we did not observe a chemoselective reaction, and an inseparable complex mixture of two mono-arylated and diarylated products was obtained. The aryl bromide **25** reacted with 2.5 equivalents of 4-ethyl-2-methylthiazole allowing the formation of the unsymmetrical 1,3-diheteroarylbenzene **31** in 84% yield. No major electronic effect of the aryl bromide was found in this reaction as 5-bromo-2-methoxybenzenesulfonyl chloride displays a similar reactivity than 5-bromo-2-methylbenzenesulfonyl chloride. Indeed, both unsymmetrical compounds **32** and **33** were synthesized in high yields. It is important to note that no homocoupling products of **26** and **27** resulting from an activation of pyrrolyl or benzofuranyl C–H bonds were detected in the crude samples.

Scheme 5. Scope of the Pd-catalyzed direct arylation with 1-bromo-3-heteroarylbenzene derivatives



3. Conclusion

In summary, we have developed two new routes for the eco-friendly two steps synthesis of unsymmetrical 1,3-diheteroarylbenzenes. The first strategy uses a desymmetrization of benzene-1,3-disulfonyl dichloride through two successive Pd-catalyzed desulfitative direct arylations of heteroarenes. The key to stop the reaction at the monoarylation stage lies in the use of diethyl carbonate (DEC) as solvent or to perform the reaction at a moderate reaction temperature. A wide range of heteroarenes has been used including thiophenes, with which the arylation occurred at the β-position. Then, a second desulfitative arylation with a different heteroarene delivered the desired 1,3-disubstituted benzenes. The second strategy employs the tolerance to C–Br bonds in the desulfitative coupling to perform iterative C–H arylations with two different heteroarenes. The combination of both strategies gives a robust access to uncommon 1,3-diheteroarylbenzenes, which could find further applications as tridentate ligands.

4. Experimental Section

All reactions were carried out under argon atmosphere with standard Schlenk techniques. 1,4-Dioxane, diethyl carbonate (DEC), cyclopentylmethyl ether (CPME) and DMA were purchased from Acros Organics and were not purified before use. 1,3-Benzenedisulfonyl chloride was purchased from TCI. The other benzenesulfonyl chlorides were prepared from bromobenzene by chlorosulfonylation (HSO_3Cl) using a reported procedure.[21] ^{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 (7.26 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.

Preparation of the PdCl(dppb)(C_3H_5) catalyst:[22] 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 yellow powder was used without purification. ^{31}P NMR (81 MHz, $CDCl_3$) δ (ppm) = 19.3 (s).

Procedure A (desulfitative arylation): To a 5 mL oven dried Schlenk tube, arylsulfonyl chloride (1.2 or 1 mmol), heteroarenes derivatives (1-3 mmol), Li_2CO_3 (222 mg, 3 mmol or 444 mg, 6 mmol), 1,4-dioxane or DEC (3 mL) and bis(acetonitrile)dichloropalladium(II) (12 mg, 0.05 mmol) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 110 or 140 °C (oil bath temperature) for 16-48 hours (see tables and schemes). After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired arylated products.

Procedure B (direct arylation with aryl bromides): To a 5 mL oven dried Schlenk tube, heteroaryl (2.5-3 mmol), aryl bromide (1 mmol), AcOK (200 mg, 2 mmol), DMA (2 mL) and $PdCl(C_3H_5)$(dppb) (12 mg, 0.02 mmol, 2 mol%) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 150 °C (oil bath temperature) for 16-48 hours (see tables and schemes). After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired arylated products.

3-(5-Butylfuran-2-yl)benzenesulfonyl chloride (1): Following the procedure **A** using 2-*n*-butylfuran (124 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **1** (260 mg, 87%).

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.23 (s, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.58 (t, *J* = 7.9 Hz, 1H), 6.72 (d, *J* = 3.3 Hz, 1H), 6.13 (d, *J* = 3.3 Hz, 1H), 2.71 (t, *J* = 7.1 Hz, 2H), 1.69 (quint., *J* = 7.2 Hz, 2H), 1.43 (sext., *J* = 7.2 Hz, 2H), 0.97 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 157.0, 151.1, 137.6, 132.1, 129.3, 125.9, 122.7, 122.3, 107.0, 106.6, 30.2, 27.9, 22.3, 13.8.

Elemental analysis: calcd (%) for $C_{14}H_{15}ClO_3S$ (298.78): C 56.28, H 5.06; found: C 56.35, H 5.29.

1,3-Bis(5-butylfuran-2-yl)benzene (2): Following the procedure **A** using 2-*n*-butylfuran (252 mg, 3 mmol) and benzene-1,3-disulfonyl dichloride (275 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 95:05) to afford the desired compound **2** (271 mg, 84%).

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.91 (s, 1H), 7.51 (d, *J* = 7.8 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 1H), 6.62 (d, *J* = 3.2 Hz, 2H), 6.10 (d, *J* = 3.2 Hz, 2H), 2.73 (t, *J* = 7.4 Hz, 4H), 1.72 (quint, *J* = 7.4 Hz, 4H), 1.46 (sext, *J* = 7.4 Hz, 4H), 0.99 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 156.6, 152.0, 131.6, 128.8, 121.8, 118.2, 106.8, 106.0, 30.2, 27.9, 22.3, 13.8.

Elemental analysis: calcd (%) for $C_{22}H_{26}O_2$ (322.45): C 81.95, H 8.13; found: C 82.17, H 8.01.

2-(3-Bromophenyl)-5-*n*-butylfuran (3): To a 5 mL oven dried Schlenk tube, 2-*n*-butylfuran (124 mg, 1 mmol), 1,3-dibromobenzene (1180 mg, 5 mmol), AcOK (100 mg, 1 mmol), DMA (2 mL) and $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol%) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 150 °C (oil bath temperature) for 16hours. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography (SiO_2, Pentane-AcOEt 90:10) to afford the desired arylated product **3** (145 mg, 52%).

^1H NMR (400MHz, $CDCl_3$) δ (ppm) 7.79 (s, 1 H), 7.56 (d, *J* = 8.2 Hz, 1 H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 6.58 (d, *J* = 3.2 Hz, 1H), 6.09 (d, *J* = 3.2 Hz, 1H), 2.71 (t, *J* = 7.4 Hz, 2H), 1.69 (quint., *J* = 7.4 Hz, 2H), 1.43 (sext., *J* = 7.4 Hz, 2 H), 0.98 (t, *J* = 7.4 Hz, 3H).

This is a known compound and the spectral data are identical to those reported in literature.[16]

3-(5-(2-Oxopropyl)furan-2-yl)benzenesulfonyl chloride (4): Following the procedure **A** using 1-(furan-2-yl)propan-2-one (124 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **4** (227 mg, 76%).

^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.24 (t, *J* = 1.9 Hz, 1H), 7.94 (td, *J* = 1.9 and 7.6 Hz, 1H), 7.88 (td, *J* = 1.9 and 7.6 Hz, 1H), 7.61 (t, *J* = 7.9 Hz, 1H), 6.80 (d, *J* = 3.4 Hz, 1H), 6.37 (d, *J* = 3.4 Hz, 1H), 3.83 (s, 2H), 2.26 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 203.1, 150.8, 149.7, 145.0, 132.4, 130.1, 129.6, 124.9, 121.6, 111.0, 108.9, 43.2, 29.5.

Elemental analysis: calcd (%) for $C_{13}H_{11}ClO_4S$ (298.74): C 52.27, H 3.71; found: C 52.49, H 4.05.

3-(Benzofuran-2-yl)benzenesulfonyl chloride (5): Following the procedure **A** using benzofuran (118 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **5** (199 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.50 (s, 1H), 8.18 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.37 (dt, *J* = 1.4 and 7.9 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.20 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.2, 152.7, 145.2, 132.5, 130.9, 130.3, 128.6, 126.1, 125.6, 123.6, 123.0, 121.6, 111.5, 104.1.

Elemental analysis: calcd (%) for $C_{14}H_9ClO_3S$ (292.73): C 57.44, H 3.10; found: C 57.69, H 3.29.

3-(1-Methylpyrrol-2-yl)benzenesulfonyl chloride (6): Following the procedure **A** using 1-methylpyrrole (81 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 90:10) to afford the desired compound **6** (189 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.08 (s, 1H), 7.95 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.66 (t, *J* = 7.9 Hz, 1H), 6.82 (t, *J* = 2.3 Hz, 1H), 6.39 (dd, *J* = 1.8 and 3.7 Hz, 1H), 6.26 (dd, *J* = 2.7 and 3.7 Hz, 1H), 3.74 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 144.5, 135.2, 134.4, 131.5, 129.7, 125.9, 125.5, 124.3, 110.6, 108.5, 35.2.

Elemental analysis: calcd (%) for $C_{11}H_{10}ClNO_2S$ (255.71): C 51.67, H 3.94; found: C 51.95, H 4.11.

3-(1-Phenylpyrrol-2-yl)benzenesulfonyl chloride (7): Following the procedure **A** using 1-phenylpyrrole (143 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **7** (219 mg, 69%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78 (d, *J* = 7.7 Hz, 1H), 7.73 (s, 1H), 7.49-7.33 (m, 5H), 7.18 (d, *J* = 8.3 Hz, 2H), 7.02 (dd, *J* = 1.7 and 2.8 Hz, 1H), 6.61 (dd, *J* = 1.7 and 3.7 Hz, 1H), 6.42 (dd, *J* = 2.8, 3.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 144.2, 139.6, 134.8, 134.0, 130.8, 129.5, 129.3, 127.5, 126.1, 125.8, 125.8, 123.8, 112.3, 109.8.

Elemental analysis: calcd (%) for $C_{16}H_{12}ClNO_2S$ (317.79): C 60.47, H 3.81; found: C 60.58, H 3.96.

3-(5-Methylthiophen-3-yl)benzenesulfonyl chloride (8): Following the procedure **A** using 2-methylthiophene (98 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **8** (158 mg, 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.17 (s, 1H), 7.90-7.85 (m, 2H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.34 (s, 1H), 7.09 (s, 1H), 2.54 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 144.9, 141.9, 139.1, 138.0, 132.6, 130.1, 124.9, 124.3, 124.1, 120.3, 14.4.

Elemental analysis: calcd (%) for $C_{11}H_9ClO_2S_2$ (272.76): C 48.44, H 3.33; found: C 48.67, H 3.58.

3-(5-Bromothiophen-3-yl)benzenesulfonyl chloride (9): Following the procedure **A** using 2-bromothiophene (163 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **9** (159 mg, 47%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.15 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.48 (s, 1H), 7.38 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 145.0, 139.8, 136.7, 132.5, 130.3, 128.6, 125.5, 124.3, 123.6, 114.3.

Elemental analysis: calcd (%) for $C_{10}H_6BrClO_2S_2$ (337.63): C 35.57, H 1.79; found: C 35.95, H 2.23.

3-(Benzothiophen-3-yl)benzenesulfonyl chloride (10): Following the procedure **A** using benzothiophene (134 mg, 1 mmol) and benzene-1,3-disulfonyl dichloride (330 mg, 1.2 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 75:25) to afford the desired compound **10** (195 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.27 (s, 1H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.98-7.94 (m, 2H), 7.86-7.81 (m, 1H), 7.75 (t, *J* = 7.9 Hz, 1H), 7.56 (s, 1H), 7.48-7.33 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 145.0, 145.0, 140.7, 138.0, 137.0, 135.2, 135.1, 130.1, 126.8, 125.7, 125.6, 125.0, 123.2, 122.1.

Elemental analysis: calcd (%) for $C_{14}H_9ClO_2S_2$ (308.79): C 54.46, H 2.94; found: C 54.18, H 3.13.

2-(3-(5-Butylfuran-2-yl)phenyl)-1-methylpyrrole (11): Following the procedure **A** using 3-(5-butylfuran-2-yl)benzenesulfonyl chloride (**1**) (299 mg, 1 mmol) and 1-methylpyrrole (203 mg, 2.5 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **11** (229 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 1H), 6.77 (t, *J* = 2.1 Hz, 1H), 6.61 (d, *J* = 3.1 Hz, 1H), 6.32 (dd, *J* = 2.0 and 3.4 Hz, 1H), 6.27 (t, *J* = 3.1 Hz, 1H), 6.11 (d, *J* = 3.1 Hz, 1H), 3.72 (s, 3H), 2.73 (t, *J* = 7.6 Hz, 2H), 1.73 (quint., *J* = 7.6 Hz, 2H), 1.46 (sext., *J* = 7.2 Hz, 2H), 1.00 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.6, 151.8, 134.4, 133.6, 131.3, 128.5, 127.0, 123.7, 123.6, 121.7, 108.7, 107.7, 106.9, 105.9, 35.0, 30.2, 27.9, 22.3, 13.8.

Elemental analysis: calcd (%) for $C_{19}H_{21}NO$ (279.38): C 81.68, H 7.58; found: C 81.51, H 7.76.

2-(3-(Benzofuran-2-yl)phenyl)-1-methylpyrrole (12): Following the procedure **A** using 3-(benzofuran-2-yl)benzenesulfonyl chloride (**5**) (293 mg, 1 mmol) and 1-methylpyrrole (203 mg, 2.5 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 70:30) to afford the desired compound **12** (200 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.95 (s, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.29-7.24 (m, 1H), 7.07 (s, 1H), 6.79 (dd, *J* = 1.8 and 2.8 Hz, 1H), 6.36 (td, *J* = 1.83 and 3.7 Hz, 1H), 6.29-6.27 (m, 1H), 3.74 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 155.7, 154.9, 134.0, 133.9, 130.6, 129.1, 128.8, 128.7, 125.1, 124.3, 123.9, 123.2, 122.9, 120.9, 111.2, 109.0, 107.9, 101.6, 35.1.

Elemental analysis: calcd (%) for $C_{19}H_{15}NO$ (273.34): C 83.49, H 5.53; found: C 83.21, H 5.19.

2-(3-(1-Methylpyrrol-2-yl)phenyl)benzoxazole (13): Following the procedure **A** using 3-(1-methylpyrrol-2-yl)benzenesulfonyl chloride (**6**) (256 mg, 1 mmol), benzoxazole (298 mg, 2.5 mmol) and CuI (190 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 70:30) to afford the desired compound **13** (187 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.32 (s, 1H), 8.20 (td, *J* = 1.9 and 7.0 Hz, 1H), 7.80 (dd, *J* = 3.1 and 6.0 Hz, 1H), 7.62-7.63 (m, 3H), 7.37 (dd, *J* = 3.2 and 6.0 Hz, 2H), 6.77 (dd, *J* = 1.8 and 2.7 Hz, 1H), 6.37 (dd, *J* = 1.8 and 3.7 Hz, 1H), 6.25 (dd, *J* = 2.7 and 3.6 Hz, 1H), 3.75 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.8, 150.7, 142.1, 134.2, 133.4, 131.4, 129.0, 127.4, 127.3, 125.7, 125.1, 124.6, 124.3, 120.0, 110.6, 109.4, 108.0, 35.2.

Elemental analysis: calcd (%) for $C_{18}H_{14}N_2O$ (274.32): C 78.81, H 5.14; found: C 79.06, H 4.87.

2-(3-(1-Phenylpyrrol-2-yl)phenyl)benzoxazole (14): Following the procedure **A** using 3-(1-phenylpyrrol-2-yl)benzenesulfonyl chloride (**7**) (318 mg, 1 mmol), benzoxazole (298 mg, 2.5 mmol) and CuI (190 mg, 1 mmol), the residue was purified by flash chromatography (SiO_2, Pentane-AcOEt 70:30) on silica gel to afford the desired compound **14** (212 mg, 63%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.22 (s, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.78 (dd, *J* = 3.0 and 6.3 Hz, 1H), 7.38-7.32 (m, 5H), 7.30 (d, *J* = 7.4 Hz, 2H), 7.23 (d, *J* = 7.4 Hz, 2H), 7.14 (d, *J* = 6.4 Hz, 1H), 7.01 (t, *J* = 2.2 Hz, 1H), 6.61 (dd, *J* = 1.8 and 3.6 Hz, 1H), 6.42 (t, *J* = 3.2 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 162.9, 150.7, 142.1, 140.3, 133.8, 132.6, 131.2, 129.1, 128.5, 127.2, 126.8, 125.8, 125.4, 125.1, 124.9, 124.5, 120.0, 111.4, 110.5, 109.4.

Elemental analysis: calcd (%) for $C_{23}H_{16}N_2O$ (336.39): C 82.12, H 4.79; found: C 82.17, H 5.01.

1-Methyl-2-(3-(1-phenylpyrrol-2-yl)phenyl)pyrrole (15): Following the procedure **A** using 3-(1-phenylpyrrol-2-yl)benzenesulfonyl chloride (**7**) (318 mg, 1 mmol) and 1-methylpyrrole (203 mg, 2.5 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 75:25) to afford the desired compound **15** (245 mg, 82%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44-7.38 (m, 2H), 7.37-7.32 (m, 2H), 7.31-7.26 (m, 4H), 7.17 (s, 1H), 7.02 (t, *J* = 2.4 Hz, 1H), 6.69 (t, *J* = 2.3 Hz, 1H), 6.56 (dd, *J* = 1.8 and 3.6 Hz, 1H), 6.46 (dd, *J* = 2.7 and 3.6 Hz, 1H), 6.21 (dd, *J* = 2.7 and 3.6 Hz, 1H), 6.13 (dd, *J* = 1.8 and 3.6 Hz, 1H), 3.39 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 140.6, 134.2, 133.5, 132.9, 129.1, 128.4, 128.3, 126.5, 126.5, 126.4, 125.8, 124.5, 123.5, 110.9, 109.3, 108.6, 107.6, 34.6.

Elemental analysis: calcd (%) for $C_{21}H_{18}N_2$ (298.39): C 84.53, H 6.08; found: C 84.72, H 5.98.

1-Methyl-2-(3-(5-methylthiophen-3-yl)phenyl)pyrrole (16): Following the procedure **A** using 3-(5-methylthiophen-3-yl)benzenesulfonyl chloride (**8**) (273 mg, 1 mmol) and 1-methylpyrrole (203 mg, 2.5 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **16** (205 mg, 81%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.62 (s, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.22 (s, 1H), 7.09 (s, 1H), 6.74 (t, *J* = 2.3 Hz, 1H), 6.29 (dd, *J* = 1.7 and 3.1 Hz, 1H), 6.24 (t, *J* = 2.8 Hz, 1H), 3.69 (s, 3H), 2.54 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 141.7, 140.5, 136.2, 134.4, 133.7, 128.6, 127.1, 126.6, 124.6, 124.5, 123.6, 118.2, 108.7, 107.8, 35.0, 15.4.

Elemental analysis: calcd (%) for $C_{16}H_{15}NS$ (253.36): C 75.85, H 5.97; found: C 76.03, H 5.78.

1,3-Bis(5-methylthiophen-3-yl)benzene (17): Following the procedure **A** using 2-methylthiophene (294 mg, 3 mmol) and benzene-1,3-disulfonyl dichloride (275 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 70:30) to afford the desired compound **17** (176 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (s, 1H), 7.48-7.44 (m, 2H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.22 (s, 2H), 7.0.9 (s, 2H), 2.54 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 142.0, 140.5, 136.6, 129.1, 124.9, 124.7, 124.3, 118.2, 15.4.

Elemental analysis: calcd (%) for $C_{16}H_{14}S_2$ (270.40): C 71.07, H 5.22; found: C 71.25, H 4.98.

1,3-Bis(1-methylpyrrol-2-yl)benzene (18): Following the procedure **A** using 1-methylpyrrole (405 mg, 5 mmol) and benzene-1,3-disulfonyl dichloride (275 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **18** (201 mg, 85%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.52-7.51 (m, 1H), 7.49-7.46 (m, 2H), 7.41-7.39 (m, 1H), 6.80-6.79 (m, 2H), 6.34-6.33 (m, 2H), 6.29-6.28 (m, 2H), 3.76 (s, 6H).

This is a known compound and the spectral data are identical to those reported in literature.[23]

1,3-Bis(1-benzylpyrrol-2-yl)benzene (19): Following the procedure **A** using 1-benzylpyrrole (786 mg, 5 mmol) and benzene-1,3-disulfonyl dichloride (275 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **19** (307 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.34 (s, 1H), 7.29-7.27 (m, 2H), 7.25-7.20 (m, 7H), 6.95 (dd, *J* = 1.7 and 7.5 Hz, 4H), 6.72 (dd, *J* = 1.9 and 2.8 Hz, 2H), 6.25 (t, *J* = 3.0 Hz, 2H), 6.23-6.21 (m, 2H), 5.08 (s, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 138.7, 134.6, 133.4, 129.2, 128.6, 128.4, 127.3, 127.3, 126.5, 123.0, 109.1, 108.5, 50.7.

Elemental analysis: calcd (%) for $C_{28}H_{24}N_2$ (388.51): C 86.56, H 6.23; found: C 86.79, H 6.31.

1,1'-(1,3-Phenylenebis(furan-5,2-diyl))bis(propan-2-one) (20): Following the procedure **A** using 1-(furan-2-yl)propan-2-one (372 mg, 3 mmol) and benzene-1,3-disulfonyl dichloride (275 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **20** (268 mg, 83%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (s, 1H), 7.51 (dd, *J* = 1.7 and 7.7 Hz, 2H), 7.37 (t, *J* = 77.7 Hz, 1H), 6.67 (d, *J* = 3.3 Hz, 2H), 6.31 (d, *J* = 3.3 Hz, 2H), 3.80 (s, 4H), 2.23 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 204.0, 153.3, 148.1, 131.1, 129.0, 122.5, 118.6, 110.5, 106.5, 43.5, 29.2.

Elemental analysis: calcd (%) for $C_{20}H_{18}O_4$ (322.36): C 74.52, H 5.63; found: C 74.89, H 5.37.

2-(3-(Benzofuran-2-yl)phenyl)benzofuran (21): Following the procedure **A** using benzofuran (354 mg, 3 mmol) and benzene-1,3-disulfonyl dichloride (275 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 90:10) to afford the desired compound **21** (233 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) δ 8.38 (s, 1H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.63-7.52 (m, 6H), 7.34-7.28 (m, 3H), 7.20 (s, 2H).

This is a known compound and the spectral data are identical to those reported in literature.[24]

4-(5-Bromo-2-methylphenyl)-2-methylthiophene (22): Following the procedure **A** using 2-methylthiophene (245 mg, 2.5 mmol) and 5-bromo-2-methylbenzenesulfonyl chloride (270 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **22** (126 mg, 47%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.46 (s, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.97 (s, 1H), 6.81 (s, 1H), 2.55 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 140.5, 139.5, 138.8, 134.5, 132.2, 131.9, 129.9, 126.8, 120.9, 119.1, 20.3, 15.3.

Elemental analysis: calcd (%) for $C_{12}H_{11}BrS$ (267.18): C 53.94, H 4.15; found: C 54.13, H 4.29.

2-bromo-4-(5-bromo-2-methylphenyl)thiophene (23): Following the procedure **A** using 2-bromothiophene (408 mg, 2.5 mmol) and 5-bromo-2-methylbenzenesulfonyl chloride (270 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **23** (173 mg, 52%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.40 (d, *J* = 2.3 Hz, 1H), 7.36 (dd, *J* = 2.1 and 8.1 Hz, 1H), 7.13-7.07 (m, 3H), 2.27 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 141.3, 137.5, 134.6, 132.1, 132.1, 131.1, 130.6, 124.4, 119.3, 112.3, 20.1.

Elemental analysis: calcd (%) for $C_{11}H_8Br_2S$ (332.05): C 39.79, H 2.43; found: C 39.56, H 2.57.

2-(5-Bromo-2-methylphenyl)-1-methylpyrrole (24): Following the procedure **A** using 1-methylpyrrole (203 mg, 2.5 mmol) and 5-bromo-2-methylbenzenesulfonyl chloride (270 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **24** (128 mg, 51%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.40-7.37 (m, 2H), 7.13 (d, *J* = 8.8 Hz, 1H), 6.70 (dd, *J* = 1.9 and 2.7 Hz, 1H), 6.2 (t, *J* = 3.2 Hz, 1H), 6.06 (dd, *J* = 1.9 and 3.6 Hz, 1H), 3.41 (s, 3H), 2.14 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 137.2, 135.2, 133.8, 131.7, 131.5, 130.8, 122.1, 118.8, 108.9, 107.5, 34.1, 19.6.

Elemental analysis: calcd (%) for $C_{12}H_{12}BrN$ (250.14): C 57.62, H 4.84; found: C 57.94, H 5.13.

2-(5-Bromo-2-methylphenyl)benzoxazole (25): Following the procedure **A** using benzoxazole (298 mg, 2.5 mmol) and CuI (190 mg, 1 mmol), 5-bromo-2-methylbenzenesulfonyl chloride (270 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **25** (130 mg, 45%).

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.34 (s, 1H), 7.83-7.79 (m, 1H), 7.53-7.57 (m, 1H), 7.51 (dd, *J* = 2.2 and 8.2 Hz, 1H), 7.42-7.38 (m, 2H), 7.21 (d, *J* = 8.2 Hz, 1H), 2.76 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.8, 150.2, 141.9, 137.7, 133.6, 133.3, 132.4, 127.9, 125.4, 124.6, 120.3, 119.5, 110.5, 21.8.

Elemental analysis: calcd (%) for $C_{14}H_{10}BrNO$ (288.14): C 58.36, H 3.50; found: C 58.14, H 3.88.

2-(5-Bromo-2-methoxyphenyl)benzofuran (26): Following the procedure **A** using benzofuran (295 mg, 2.5 mmol) and 5-bromo-2-methoxybenzenesulfonyl chloride (286 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15)to afford the desired compound **26** (188 mg, 62%).

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.20 (d, *J* = 2.6 Hz, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.41-7.35 (m, 2H), 7.34-7.23 (m, 2H), 6.81 (d, *J* = 8.8 Hz, 1H), 3.93 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 107.4, 110.9, 112.6, 113.2, 121.1, 121.3, 122.8, 124.6, 129.4, 129.5, 131.5, 150.6, 153.9, 155.4, 55.7.

Elemental analysis: calcd (%) for $C_{15}H_{11}BrO_2$ (303.16): C 59.43, H 3.66; found: C 59.23, H 3.61.

2-(5-Bromo-2-methoxyphenyl)-1-methylpyrrole (27): Following the procedure **A** using 1-methylpyrrole (203 mg, 2.5 mmol) and 5-bromo-2-methoxybenzenesulfonyl chloride (286 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **27** (197 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.49-7.44 (m, 2H), 6.87 (d, *J* = 8.2 Hz, 1H), 6.77 (t, *J* = 2.3 Hz, 1H), 6.26 (t, *J* = 2.9 Hz, 1H), 6.20 (dd, *J* = 2.0 and 3.6 Hz, 1H), 3.83 (s, 3H), 3.53 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 156.4, 134.6, 131.5, 129.5, 124.6, 122.9, 112.5, 112.4, 109.4, 107.6, 55.6, 34.5.

Elemental analysis: calcd (%) for $C_{12}H_{12}BrNO$ (266.14): C 54.16, H 4.55; found: C 54.32, H 4.38.

2-(5-bromo-2-methoxyphenyl)benzoxazole (28): Following the procedure **A** using benzoxazole (298 mg, 2.5 mmol) and CuI (190 mg, 1 mmol), 5-bromo-2-methoxybenzenesulfonyl chloride (286 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **28** (116 mg, 38%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.27 (d, *J* = 2.7 Hz, 1H), 7.85-7.81 (m, 1H), 7.62-7.57 (m, 2H), 7.40-7.33 (m, 2H), 6.98 (d, *J* = 9.1 Hz, 1H), 4.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 159.9, 157.5, 135.3, 133.6, 125.4, 124.5, 120.4, 117.9, 113.9, 112.8, 110.5, 56.5.

Elemental analysis: calcd (%) for $C_{14}H_{10}BrNO_2$ (304.14): C 55.29, H 3.31; found: C 55.63, H 3.18.

2-(4-Methyl-3-(5-methylthiophen-3-yl)phenyl)benzoxazole (29): Following the procedure **B** using benzoxazole (298 mg, 2.5 mmol) and 4-(5-bromo-2-methylphenyl)-2-methylthiophene (**22**) (267 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **29** (223 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.19 (s, 1H), 8.09 (dd, *J* = 1.9 and 7.9 Hz, 1H), 7.77 (dd, *J* = 2.9 and 4.5 Hz, 1H), 7.58-7.54 (m, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.36-7.321 (m, 2H), 7.06 (s, 1H), 6.82 (s, 1H), 2.55 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 163.1, 150.6, 142.1, 140.8, 139.7, 139.5, 137.6, 131.1, 128.7, 127.0, 126.1, 124.9, 124.7, 124.5, 121.0, 119.8, 110.4, 21.0, 15.3.

Elemental analysis: calcd (%) for $C_{19}H_{15}NOS$ (305.40): C 74.73, H 4.95; found: C 74.62, H 5.12.

2-(4-methyl-3-(1-methylpyrrol-2-yl)phenyl)benzoxazole (30): Following the procedure **B** using benzoxazole (298 mg, 2.5 mmol) and 2-(5-bromo-2-methylphenyl)-1-methylpyrrole (**24**) (250 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **30** (228 mg, 79%).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.18-8.15 (m, 2H), 7.78-7.75 (m, 1H), 7.58-7.54 (m, 1H), 7.44 (d, *J* = 8.5 Hz, 1H), 7.37-7.32 (m, 2H), 6.75 (dd, *J* = 1.8 and 2.7 Hz, 1H), 6.25 (dd, *J* = 2.7 and 3.5 Hz, 1H), 6.15 (dd, *J* = 1.8 and 3.5 Hz, 1H), 3.47 (s, 3H), 2.30 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 163.0, 150.7, 142.3, 142.1, 134.0, 132.0, 130.7, 130.3, 126.9, 124.9, 124.6, 124.5, 122.1, 119.9, 110.5, 109.0, 107.5, 34.2, 20.3.

Elemental analysis: calcd (%) for $C_{19}H_{16}N_2O$ (288.35): C 79.14, H 5.59; found: C 78.95, H 5.41.

2-(5-(4-ethyl-2-methylthiazol-5-yl)-2-methylphenyl)benzoxazole (32): Following the procedure **B** using 4-ethyl-2-methylthiazole (318 mg, 2.5 mmol) and 2-(5-bromo-2-methylphenyl)benzoxazole (**25**) (288 mg, 1 mmol), the

residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 85:15) to afford the desired compound **31** (281 mg, 84%).

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.23 (d, *J* = 1.9 Hz, 1H), 7.85-7.78 (m, 1H), 7.63-7.58 (m, 1H), 7.45 (dd, *J* = 1.9 ans 7.9 Hz, 1H), 7.40 (s, 1H), 7.39-7.35 (m, 2H), 3.03 (q, *J* = 7.6 Hz, 2H), 2.84 (s, 3H), 2.51 (s, 3H), 1.42 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4, 162.7, 150.3, 147.4, 142.1, 138.2, 132.2, 131.3, 130.4, 129.8, 126.6, 125.2, 124.5, 120.2, 110.5, 26.9, 21.9, 16.1, 14.3.

Elemental analysis: calcd (%) for $C_{20}H_{18}N_2OS$ (334.44): C 71.83, H 5.43; found: C 72.13, H 5.28.

4-Ethyl-5-(4-methoxy-3-(1-methylpyrrol-2-yl)phenyl)-2-methylthiazole (32): Following the procedure **B** using 4-ethyl-2-methylthiazole (318 mg, 2.5 mmol) and 2-(5-bromo-2-methoxyphenyl)-1-methylpyrrole (**27**) (266 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **32** (247 mg, 79%).

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.43-7.34 (m, 2H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.75 (dd, *J* = 1.8 and 2.8 Hz, 1H), 6.24 (dd, *J* = 2.8 and 3.5 Hz, 1H), 6.18 (dd, *J* = 1.8 and 3.5 Hz, 1H), 3.85 (s, 3H), 3.54 (s, 3H), 3.01 (q, *J* = 7.6 Hz, 2H), 2.48 (s, 3H), 1.41 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 169.6, 156.7, 146.4, 132.9, 130.4, 130.3, 129.7, 124.7, 122.8, 122.7, 110.8, 109.2, 107.6, 55.5, 34.6, 26.9, 16.0, 14.3.

Elemental analysis: calcd (%) for $C_{18}H_{20}N_2OS$ (312.43): C 69.20, H 6.45; found: C 69.47, H 6.59.

5-(3-(Benzofuran-2-yl)-4-methoxyphenyl)-4-ethyl-2-methylthiazole (33): Following the procedure **B** using 4-ethyl-2-methylthiazole (318 mg, 2.5 mmol) and 2-(5-bromo-2-methoxyphenyl)benzofuran (**26**) (303 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (SiO_2, Pentane-AcOEt 80:20) to afford the desired compound **33** (300 mg, 86%).

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.12 (d, *J* = 2.3 Hz, 1H), 7.61 (dd, *J* = 1.5 and 7.5 Hz, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 0.9 Hz, 1H), 7.35 (dd, *J* = 2.4 and 8.5 Hz, 1H), 7.29 (dt, *J* = 1.5 and 7.0 Hz, 1H), 7.23 (dt, *J* = 1.5 and 7.0 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 1H), 4.03 (s, 3H), 3.03 (q, *J* = 7.6 Hz, 2H), 2.50 (s, 3H), 1.43 (t, *J* = 7.6 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 169.8, 155.9, 153.9, 151.4, 146.8, 130.3, 129.8, 129.6, 127.8, 125.0, 124.3, 122.7, 121.1, 119.5, 111.2, 110.9, 106.9, 55.6, 26.9, 16.0, 14.3.

Elemental analysis: calcd (%) for $C_{21}H_{19}NO_2S$ (349.45): C 72.18, H 5.48; found: C 72.35, H 5.67.

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19 Suprisingly, the arenesulfonyl chloride **1** is quite stable and could be purified over regular silica gel without hydrolysis of the sulfonyl chloride function.

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