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Eco-Friendly Solvents for Palladium-Catalyzed Desulfitative C–H Bond Arylation of Heteroarenes

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Herein, we report the Pd-catalyzed regioselective direct arylation of heteroarenes in which benzenesulfonyl chlorides are used as coupling partners through a desulfitative cross-coupling that can be performed in diethyl carbonate (DEC) or cyclopentyl methyl ether (CPME) as green and renewable solvents or even in neat conditions instead of dioxane or dimethylacetamide (DMA). Under these solvent conditions, the reaction proceeds with a wide range of heteroarenes. C2- or C5-arylated products were obtained with furan and pyrrole derivatives. Benzofuran was also arylated regioselectively at the C2-position, whereas the reaction proceeds selectively at the C3- or C4-positions if thiophenes and benzothiophenes are used. Moreover, in some cases, especially with 1-methylindole, solvent-free conditions afforded better regioselectivities and/or yields than the reaction performed in the presence of solvents.

Introduction

The discovery of green chemistry processes is a great challenge and hot topic from both academic and industrial points of views.[1] Indeed, the simplification of chemical processes along with the decrease of waste and cost is an important ideal for human development. In this line, the catalytic direct functionalization of C–H bonds has emerged recently as one of the most promising and powerful methods for the construction of C–C bonds because of the generation of lower amounts of waste compared to that of traditional useful cross-couplings.[2] Among diverse protocols for C–H bond cross-coupling, the Pd-catalyzed direct arylation of (hetero)arenes through C(sp^2)–H bond activation is under constant investigation. Since the discovery of Ohta and co-workers in 1985–1992 of the direct C2- or C5-arylation of several heteroaromatics with aryl halides in which $Pd(PPh_3)_4$ was used as the catalyst and dimethylacetamide (DMA) as the solvent,[3,4] the direct arylation of heteroaromatics has promoted a large effort from chemists because of the biological and physical properties of such aryl-heteroaryl derivatives.[5]

Recently, our group and others disclosed that benzenesulfonyl chlorides can be used as suitable and original coupling partners in the Pd-catalyzed direct arylation of heteroarenes.[6] The first example of such a direct desulfitative-coupling was reported by Dong and co-workers in 2009, who arylated benzoquinoline in high yield using a Pd catalyst in the presence of Ag and Cu salts in dioxane (Figure 1 A).[7] The arylation of benzoxazole was performed by Cheng et al. who used similar reaction conditions in dioxane, although they used K_2CO_3 instead of Ag_2CO_3 (Figure 1 B).[8] Then, Jafarpour and co-workers described the Pd-catalyzed direct desulfitative arylation of coumarins in the presence of Cu salts in dioxane and the direct desulfitative arylation of pyrrole in dimethylacetamide (DMA; Figure 1 C).[9] Recently, we described the direct arylation of several heteroarenes, such as (benzo)furans,[10] (benzo)thiophenes,[11] and pyrroles,[12] through a desulfitative cross-coupling reaction (Figure 1 D). Sodium sulfinates have been also used in desulfitative direct arylations for the arylation of various heteroarenes[13] The reaction proceeded in high yields if 5 mol% $PdCl_2(CH_3CN)_2$ was used in the presence of lithium carbonate (Li_2CO_3), sometimes with unexpected regioselectivities.[11] The advantages of RSO_2Cl derivatives over arene sulfinates, arylsulfonyl hydrazides, diaryliodonium salts, or boronic acids are that many of them are commercially available and easy to handle. They can be prepared easily from sulfonic acids or sulfur substrates by chlorination.[14] Moreover, the generation of SO_2 is not an important issue for industrial processes as SO_2 is added in small amounts to some beverages and foods as a preservative.

The major drawback of such reactions in terms of green chemistry is that the solvents employed are toxic or not eco-friendly (e.g., dioxane or DMA) according to solvent selection guides described by chemical companies.[15] In organic reactions, the solvent is generally the chemical used in the largest excess, which consequently generates the largest amount of waste. To develop greener processes, specific attention should be paid to the choice and amount of the solvent and its compatibilities with the catalyst.

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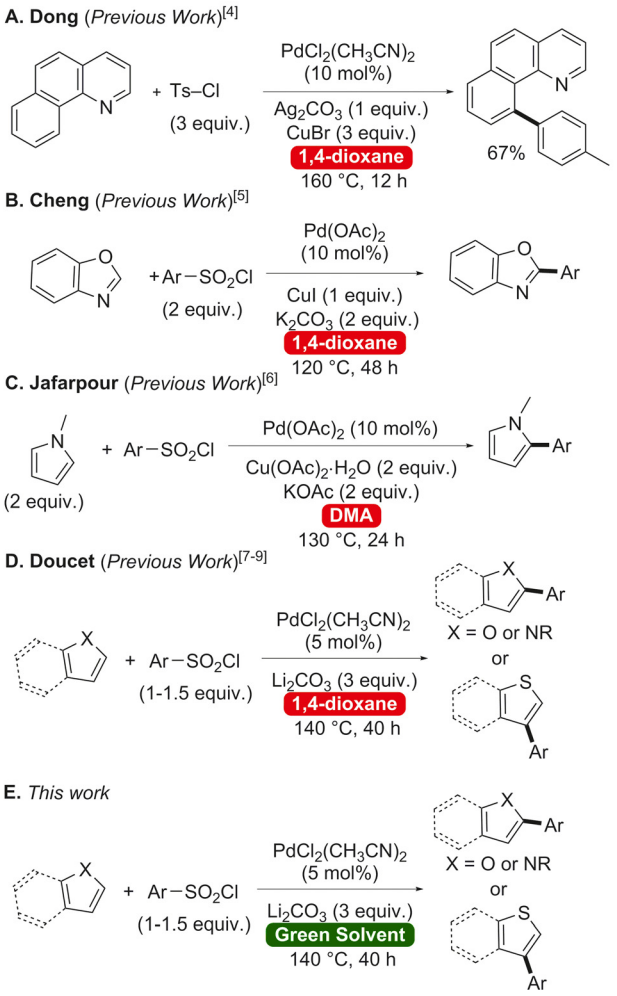


Figure 1. Previous examples of Pd-catalyzed desulfitative C–H bond arylations in which benzenesulfonyl chlorides are used as coupling partners.

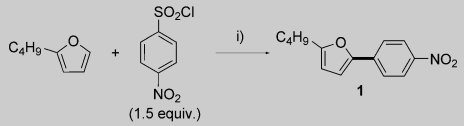
Carbonates, such as diethyl carbonate (DEC) are polar, aprotic, nontoxic, and biodegradable solvents.[16] Based on these properties, carbonates should offer an environmentally friendly alternative to standard polar solvents. Carbonates have been employed successfully for some classical metal-catalyzed reactions such as enantioselective hydrogenation,[17] alkene metathesis,[18] carbonylation,[19] oxidation,[20] hydroxylation,[21] Sonogashira coupling,[22] Heck vinylation or allylic alkylation,[23] and C–H bond activation/functionalization.[24] Cyclopentyl methyl ether (CPME) is a suitable alternative solvent to other ethers such as THF or dioxane because of its high hydrophobicity—its limited miscibility in water allows easy separation and recovery from water and reduces the waste stream—low formation of peroxides (compared with THF and diisopropyl ether), relative stability under acidic and basic conditions, and narrow explosion range. CPME can be manufactured by the addition of MeOH to cyclopentene, which produces no apparent waste.[25] Moreover, metal-catalyzed reactions have already been performed in CPME,[26] which include C–H bond arylation.[27] Reactions performed under solvent-free conditions have several advantages compared to the use of toxic and hazardous chemicals such as a reduction of waste, a reduction in reactor size, and simpler workup.[28] However, to the best of our knowledge, carbonates, CPME, or solvent-free conditions have not been yet employed for Pd-catalyzed direct arylations through desulfitative cross-coupling in which benzenesulfonyl chlorides are used as arylating agents. The use of these conditions would provide a cost-effective and environmentally attractive procedure for the preparation of arylated heteroarenes.

Herein, we report the influence of DEC or CPME for the Pd-catalyzed direct desulfitative arylation of a wide range of heteroaromatic derivatives. Reactions under neat conditions were also performed (Figure 1 E).

Results and Discussion

Firstly, we selected commercially available 2-*n*-butylfuran and 4-nitrobenzenesulfonyl chloride as model substrates and applied our previous best conditions,[10b] that is, 5 mol% $PdCl_2(CH_3CN)_2$ in the presence of 3 equivalents of Li_2CO_3 in dioxane at 140 °C for 40 h. Under these conditions the C2-arylation product **1** was obtained in 88% yield (Table 1, entry 1).

Table 1. Solvent screening for the Pd-catalyzed direct desulfitative arylation of 2-*n*-butylfuran with 4-nitrobenzenesulfonyl chloride.



i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), solvent, 140 °C, *t* [h]

Entry	Solvent (conc. [mol L^{-1}])	*t* [h]	Conversion[a,b] [%]	Yield of **1**[a] [%]
1	dioxane (0.33)	40	100	88
2	ethylene glycol (0.33)	40	100	0
3	pentan-1-ol (0.33)	40	100	0
4	water (0.33)	40	100	0
5	CPME (0.5)	40	100	64
6[c]	DMC (0.5)	40	100	trace
7	DEC (0.5)	40	65	58
8	DEC (1)	40	100	90
9	DEC (1)	15	100	95 (88)
10	PC (0.5)	40	100	0
11	DEC/water (5:1; 0.5)	40	100	0
12	DEC/pentanol (5:1; 0.5)	40	100	0
13	neat	15	100	95 (85)

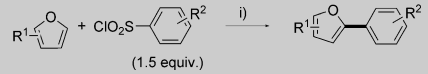
[a] Determined by ^{1}H NMR spectroscopy. The number in parentheses shows the isolated yield. [b] Based on 4-nitrobenzenesulfonyl chloride. [c] Reaction performed at 100 °C. PC = propylene carbonate.

Then, we screened greener solvents using these conditions. No formation of the desired product **1** was observed in protic polar solvents such as ethylene glycol, pentan-1-ol, or water; and only the degradation of the benzenesulfonyl chloride derivative was observed (Table 1, entries 2–4). CPME affords the desired C5-arylation product **1** in 64% yield (Table 1, entry 5).

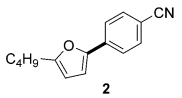
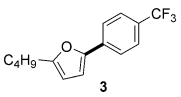
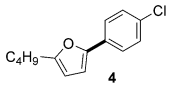
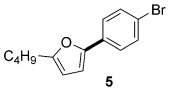
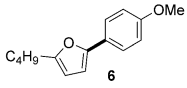
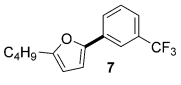
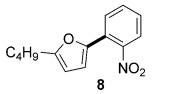
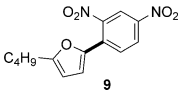
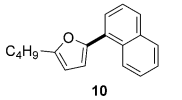
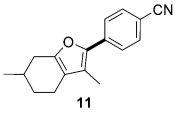
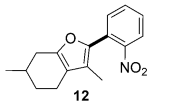
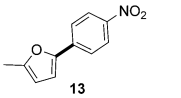
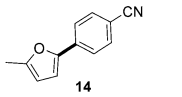
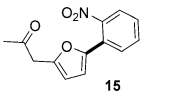
The reaction conducted in dimethylcarbonate (DMC) at 100 °C—because of the low boiling point of this solvent (90 °C)—gave only a trace amount of the desired compound **1** (Table 1, entry 6). Next, we decided to switch to DEC, which has a higher boiling point (126–128 °C) than DMC, and performed the reaction at 140 °C in 0.5 M. Under these conditions, **1** was obtained in 58% yield after 40 h without the full consumption of benzenesulfonyl chloride (Table 1, entry 7). A higher concentration of 1 mol L^{-1} allowed the full conversion of benzenesulfonyl chloride and gave **1** in 90% yield (Table 1, entry 8). If we used DEC at 1 mol L^{-1}, the reaction time was decreased to 15 h without an effect on the yield (Table 1, entry 9). Propylene carbonate was also tested, however, the desired product **1** was not detected (Table 1, entry 10). A mixture of DEC with a protic solvent such as water or pentan-1-ol to favor the solubilization of the inorganic base only gave the degradation of the benzenesulfonyl chloride (Table 1, entries 11 and 12). Finally, neat conditions also provide the desired product **1** in a high isolated yield of 85% (Table 1, entry 13).

After we had determined that DEC is the best green solvent for such desulfitative cross-coupling reactions, we next focused on the scope and limitation for the direct C5-arylation of furan derivatives (Table 2). Firstly, the influence of the substituents on the benzenesulfonyl chloride partners for the coupling with 2-*n*-butylfuran was examined using 5 mol% $Pd(MeCN)_2Cl_2$ catalyst and Li_2CO_3 as base in DEC at 140 °C for 15 h. The reaction proceeded smoothly with a wide range of benzenesulfonyl chlorides that bear electron-withdrawing groups such as $-NO_2$, $-CN$, $-CF_3$, $-Cl$, and $-Br$ at the *para* position, and the C5-arylation products **1**–**5** were isolated in good to excellent yields. Moreover, the synthesis of **5** was also conducted with a moderate 64% yield in CPME and with a high yield of 92% using solvent-free conditions. Notably, under all these reaction conditions, the C–Br bond was not involved in the arylation reaction, which allowed further transformations. However, with an electron-donating substituent at the *para* position, such as $-OMe$, only trace amounts of **6** were observed, even using a reaction time longer than 40 h. A *meta*-substituted benzenesulfonyl chloride was also tolerated and gave the desired product **7** in 48% yield. The reaction was not affected by steric hindrance, as **8** with a NO_2 substituent at the *ortho* position was isolated in 81% yield. However, the presence of two NO_2 substituents on the benzenesulfonyl chloride partner afforded the desired C5-arylated product **9** in a lower yield. The less reactive naphthalene-1-sulfonyl chloride reacted over a longer time (40 h) to provide the desired C5-arylation product **10** in 55% yield. Next, the reactivity of other furan derivatives was examined. Menthofuran showed high reactivity with activated benzenesulfonyl chloride to give the desired desulfitative cross-coupling products **11** and **12** in 82 and 65% yield, respectively. The reaction was also performed using 2-methylfuran as the substrate. This was undertaken in an autoclave because of the low boiling point of this furan (63–66 °C). The C5-arylated 2-methylfurans **13** and **14** were isolated in 67 and 48% yield, respectively. A furan that bears a ketone function at the C2-position, 1-(furan-2-yl)propan-2-one, also reacted well to afford the C5-arylated product **15** in 76% yield. Other solvent conditions, namely, CPME and neat conditions, displayed a similar activity for the C5-arylation of 1-(furan-2-yl)propan-2-one, as **15** was isolated in 78 and 84% yield, respectively.

Table 2. Scope of benzenesulfonyl chlorides in the Pd-catalyzed desulfitative arylation of furan derivatives.



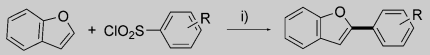
i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), DEC, 140 °C, *t* [h]

Product	Yield [%]	*t* [h]	Product	Yield [%]	*t* [h]
 **2**	91	15	 **3**	90	15
 **4**	64	15	 **5**	89 (64[a], 92[b])	15
 **6**	trace	40	 **7**	48	15
 **8**	81	15	 **9**	46	15
 **10**	55	40	 **11**	82	15
 **12**	65	15	 **13**	67	40[c]
 **14**	48	40[c]	 **15**	76 (78[a], 84[b])	40

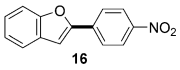
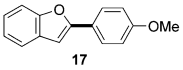
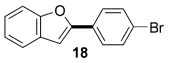
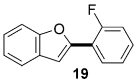
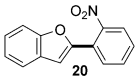
[a] Reaction performed in CPME. [b] Reaction performed in neat conditions. [c] $ArSO_2Cl$ (1 equiv.), HetArH (2 equiv.); reaction performed using an autoclave.

Then, the C2 direct arylation of benzofuran in DEC was investigated. The reaction proceeded smoothly, but a longer reaction time of 40 h was required to reach the full consumption of the benzenesulfonyl chloride (Table 3). From benzofuran, **16** was obtained in a high yield with 4-nitrobenzenesulfonyl chloride. If we used the less reactive 4-methoxybenzenesulfonyl chloride, which is not reactive with 2-*n*-butylfuran (Table 2), the desulfitative cross-coupling product **17** was isolated in 38% yield. Interestingly, the reaction gave a higher yield if CPME was used as the solvent instead of DEC, whereas only trace amounts of **17** were obtained under neat conditions. Again, the reaction conditions were found to tolerate the bromo functional group. For example, **18** was isolated in 78% yield from 4-bromobenzenesulfonyl chloride. Other solvent conditions, namely, CPME or neat conditions, also allowed the formation of **18** in 83 and 57% yield, respectively. The reaction is

Table 3. Scope of benzenesulfonyl chlorides in the Pd-catalyzed desulfitative arylation of benzofuran.



i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), DEC, 140 °C, 40 h

Product	Yield [%]	Product	Yield [%]
 **16**	83	 **17**	38 (58[a], trace[b])
 **18**	79 (83[a], 57[b])	 **19**	84
 **20**	52		

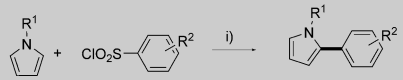
[a] Reaction performed in CPME. [b] Reaction performed in neat conditions.

slightly sensitive to steric hindrance. For example, the reaction of 2-fluorobenzenesulfonyl chloride or 2-nitrobenzenesulfonyl chloride gave the desired arylated products **19** and **20** in 84 and 52% yield, respectively.

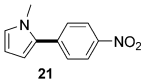
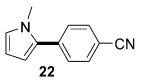
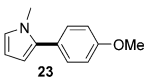
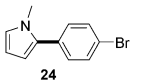
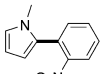
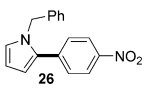
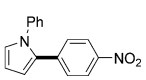
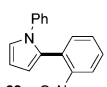
Pyrroles were arylated regio- and chemoselectively at the C2-position using benzenesulfonyl chloride derivatives in DEC (Table 4), but 2 equivalents of pyrrole derivatives were used to prevent the formation of diarylation products. From 1-methylpyrrole and 4-nitro- or 4-cyanobenzenesulfonyl chlorides, the C2-arylated pyrroles **21** and **22** were isolated in high yields after only 15 h. In contrast to the reaction with (benzo)furans, 1-methylpyrrole was arylated using 4-methoxybenzenesulfonyl chloride in good yield. However, in the crude mixture, we also observed the formation of a large amount of the C2,C5-diarylation product. If the reaction was performed in CPME, the arylated product **23** was isolated in a slightly higher yield because of the decreased amount of the C2,C5-diarylation product. In contrast, under neat conditions, the desulfitative-coupling product **23** was obtained in a low yield because of the formation of a larger amount of C2,C5-diarylation product. Again, the reaction proceeded well with 4-bromobenzenesulfonyl chloride to allow the formation of **24** in 75% yield. Other solvents displayed a similar reactivity; for example, **24** was isolated in 77% yield in CPME and 80% under neat conditions. As in the case of the arylation of benzofuran, the arylation of pyrroles tolerated an *ortho* substituent on the benzene sulfonyl chloride reagent. The reaction of 1-methylpyrrole with 2-nitrobenzenesulfonyl chloride provided aryl pyrrole **25** in 86% yield. Other substituents on the nitrogen atom, such as benzyl or phenyl, gave the corresponding coupling products **26**, **27**, and **28** in 87, 73, and 73% yield, respectively.

Next, we investigated the direct desulfitative arylation of 1-methylindole.[13f,29] The use of 4-bromobenzenesulfonyl chloride in dioxane gives a mixture of arylation products at the 2- or 3-position (**29a**/**29b**) in a 51:49 ratio, albeit with a moderate conversion (Table 5, entry 1). Interestingly, we found that the solvent has a huge effect on the regioselectivity of this reaction. Indeed, if the reaction was performed in DEC instead of dioxane, the regioisomer **29b** was obtained as the major product (Table 5, entry 2), whereas the reaction in CPME gave almost an equimolar mixture of the two regioisomers. Finally, using solvent-free conditions, the regioisomer **29a**, in which the arylation took place at the C2-position, was obtained in an excellent ratio of 85:15 and was isolated in 62% yield (Table 5, entry 4).

Table 4. Scope of benzenesulfonyl chlorides in the Pd-catalyzed desulfitative arylation of pyrrole derivatives.

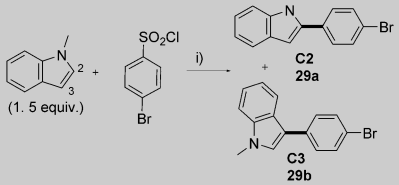


i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), DEC, 140 °C, 15 h

Product	Yield [%]	Product	Yield [%]
 **21**	92	 **22**	89
 **23**	48[a] (55[a,b], 23[a,c])	 **24**	75 (71[b,d], 65[c,d])
 **25**	86	 **26**	87
 **27**	73	 **28**	73

[a] Presence of 2,5-bis(4-methoxyphenyl)-1-methylpyrrole in the crude mixture: [b] Reaction performed in CPME. [c] Reaction performed in neat conditions. [d] Trace of 2,5-bis(4-bromophenyl)-1-methylpyrrole.

Table 5. Pd-catalyzed desulfitative direct arylation of 1-methylindole with 4-bromobenzenesulfonyl chloride: effect of the solvent on the regioselectivity.



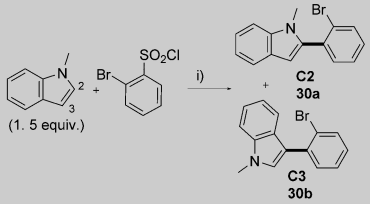
i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), 140 °C, 24 h

Entry	Solvent	Conversion[a] [%]	**29a**/**29b**[a]
1	dioxane	49	51:49
2	DEC	44	34:66 (29%[b])
3	CPME	46	49:51
4	neat	73	85:15 (62%[c])

[a] Determined from the ^{1}H NMR spectrum of the crude product. [b] Isolated yield of **29b**. [c] Isolated yield of **29a**.

Previously, we found that the reaction with 1-methylindole in dioxane is very sensitive to the steric hindrance of the benzenesulfonyl chloride partner,[12] so we decided to investigate the regioselectivity of this reaction with 2-bromobenzenesulfonyl chloride under different solvent conditions. Again, the solvent was critical for both regioselectivity and conversion (Table 6, entries 1–4). Quasi-equimolar ratios between the two regioisomers **30a** and **30b** were obtained in CPME and DEC, albeit in a poor conversion of 26 and 41%, respectively (Table 6, entries 2 and 3). The reaction performed in dioxane showed a slightly higher regioselectivity in favor of **30a** but with a low conversion of 31% (Table 6, entry 1). Finally, under solvent-free conditions, the reaction was complete with a high regioselectivity in favor of **30a**, which was isolated in 71% yield (Table 6, entry 4).

Table 6. Pd-catalyzed desulfitative direct arylation of 1-methylindole with 3-bromobenzenesulfonyl chloride: effect of the solvent and steric hindrance on the regioselectivity.



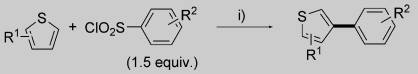
i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), 140 °C, 24 h

Entry	Solvent	Conversion[a] [%]	**30a**/**30b**[a]
1	dioxane	31	77:23
2	DEC	26	55:45
3	CPME	41	52:48
4	neat	95	80:20 (71%[b])

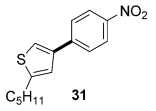
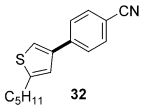
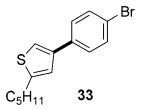
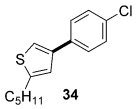
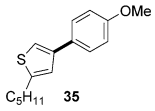
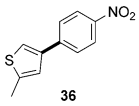
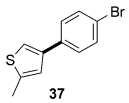
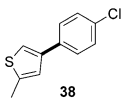
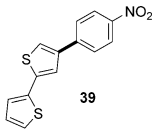
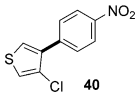
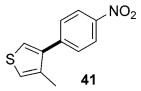
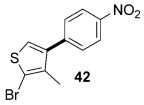
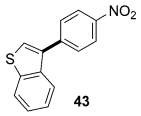
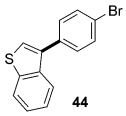
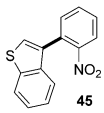
[a] Determined from the ^{1}H NMR spectrum of the crude product. [b] Isolated yield of **30a**.

Then, we turned our attention to thiophene derivatives. We found previously that in dioxane the arylation occurs at the unexpected C3-position in the presence of 5 mol% $PdCl_2(CH_3CN)_2$ as catalyst and Li_2CO_3 as base.[11] In DEC medium, the reaction proceeded similarly, and the C3-arylated thiophenes were obtained after 40 h (Table 7). Firstly, the influence of the substituents at the *para* position on the benzenesulfonyl chlorides for the coupling with 2-*n*-pentylthiophene was examined. Again, benzenesulfonyl chlorides that bear electron-withdrawing groups such as $-NO_2$, –CN, –Br, and –Cl displayed high reactivities, and the C3-arylated products **31**–**34** were isolated in 74–84% yield. If 4-nitrobenzenesulfonyl chloride and 2-*n*-pentylthiophene were used as substrates, the reaction proceed in a lower yield of 43% in CPME, whereas almost no reaction occurred under neat conditions. Similar to the reaction with (benzo)furans, an electron-donating substituent on the benzenesulfonyl chloride partner, such as 4-methoxybenzenesulfonyl chloride, inhibited the reaction, and only a trace amount of the arylated product **35** was observed. Next, the reactivity of other thiophene derivatives in DEC was surveyed. 2-Methylthiophene was arylated to provide the desired products **36**–**38** in moderate to high yields. From 2,2′-bithiophene and 4-nitrobenzenesulfonyl chloride, the mono-C3-arylated product **39** was obtained selectively in a good yield of 66%. This family of bithiophenes could allow simple access to electronic devices or materials.[30] The C4-arylation of thiophenes substituted in the 3-position was also investigated. 3-Chlorothiophene reacted poorly with 4-nitrobenzenesulfonyl chloride to give the arylated product **40** in a low yield of 35%. Notably, with this thiophene derivative, no reaction occurred in CPME or if solvent-free conditions were used. Interestingly, the C4-arylated product of 3-methylthiophene was obtained in a better yield of 79%. With the use of this thiophene, the reac-

Table 7. Scope of benzenesulfonyl chlorides in the Pd-catalyzed desulfitative arylation of thiophene derivatives.



i) $PdCl_2(CH_3CN)_2$ (5 mol%), Li_2CO_3 (3 equiv.), DEC, 140 °C, 40 h

Product	Yield [%]	Product	Yield [%]
 **31**	50 (43[a], trace[b])	 **32**	84
 **33**	74	 **34**	76
 **35**	trace	 **36**	89
 **37**	40	 **38**	73
 **39**	66	 **40**	35 (trace[a], trace[b])
 **41**	79 (64[a], trace[b])	 **42**	56
 **43**	41 (85[c])	 **44**	88[c]
 **45**	85[c]		

[a] Reaction performed in CPME. [b] Reaction performed in neat conditions. [c] Reaction performed during 72 h.

tion occurred smoothly in CPME, whereas under neat conditions only a trace amount of the arylated product **41** was obtained. A bromo substituent at the 2-position of thiophene was also tolerated, and the 4-arylated 2-halothiophene **42** was obtained in 56% yield.

Finally, the arylation of benzothiophene was investigated, and the reaction proceeds very slowly in DEC. After 40 h, only 41% yield of the coupling product **43** was obtained, because of the partial consumption of 4-nitrobenzenesulfonylchloride. 4-Nitrobenzenesulfonylchloride was consumed fully after 72 h, and the aryl thiophene **43** was isolated in 85% yield. Other benzenesulfonyl chlorides such as 4-bromobenzenesulfonyl chloride and 2-nitrobenzenesulfonyl chloride also allowed the formation of C3-arylated benzothiophenes **44** and **45** in high yields.

Conclusions

We have shown that diethyl carbonate (DEC) and in some cases cyclopentyl methyl ether (CPME), which are both considered as "green solvents", can be employed advantageously as an alternative to common solvents in the Pd-catalyzed desulfitative direct arylation of several heteroaromatic derivatives in which benzenesulfonyl chlorides are used as coupling partners. In the presence of DEC or CPME and 5 mol% $PdCl_2(CH_3CN)_2$ as the catalyst precursor at 140 °C, the direct C5-arylation of furans, the C2-arylation of benzofuran, the C2-arylation of pyrroles, and the C3-arylation of (benzo)thiophenes proceed in moderate to high yields. Notably, the reaction is chemoselective, as C–X (X = Cl, Br) bonds are not involved in the arylation process. In some cases, solvent-free conditions, which are beneficial for the reduction of waste, showed high reactivity, especially for 1-methylindole with which the arylation took place more selectively at the C2 position. The major byproducts of these couplings are LiCl and SO_2 instead of metal salts that result from more classical coupling procedures. Moreover, this method does not require an external toxic oxidant such as Ag or Cu salts. For these reasons, this new process offers economically viable and environmentally attractive access to arylated heteroaromatics. 45 examples are reported, which demonstrates the wide scope of DEC, CPME, or solvent-free conditions for the desulfitative direct arylation reaction.

Experimental Section

All reactions were performed under argon atmosphere using standard Schlenk techniques. DEC and CPME were purchased from Acros Organics and were not purified before use. ^{1}H NMR spectra were recorded by using Bruker GPX (400 MHz or 300 MHz) spectrometers. Chemical shifts (δ) were reported in ppm relative to residual chloroform (δ = 7.26 ppm for ^{1}H; δ = 77.0 ppm for ^{13}C), and coupling constants were reported in Hertz. ^{1}H NMR assignment abbreviations are 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 or 75 MHz on the same spectrometers and reported in ppm. All reagents were weighed and handled in air.

To a 5 mL oven-dried Schlenk tube, arylsulfonyl chloride (1–1.5 mmol), heteroarene derivatives (1–2 mmol), Li_2CO_3 (0.222 g, 3 mmol), DEC (1 mL), CPME (1 mL), or no solvent (see tables and schemes), and bis(acetonitrile)dichloropalladium(II) (12.9 mg, 0.05 mmol) were added successively. The reaction mixture was evacuated by vacuum–argon cycles (five times) and stirred at 140 °C (oil bath temperature) for 15–72 h (see tables and schemes). After cooling the reaction to RT and concentration, the crude mixture was purified by silica column chromatography to afford the desired arylated products.

2-*n*-Butyl-5-(4-nitrophenyl)furan (1)[5b]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **1** in 88% (0.216 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 6.68 (d, J = 3.2 Hz, 1H), 6.05 (d, J = 3.2 Hz, 1H), 2.61 (t, J = 7.4 Hz, 2H), 1.58 (quint., J = 7.4 Hz, 2H), 1.34 (sext., J = 7.4 Hz, 2H), 0.87 ppm (t, J = 7.4 Hz, 3H).

2-*n*-Butyl-5-(4-cyanophenyl)furan (2)[5b]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.303 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **2** in 91% (0.205 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.6 Hz, 2H), 6.61 (d, J = 3.2 Hz, 1H), 6.02 (d, J = 3.2 Hz, 1H), 2.60 (t, J = 7.4 Hz, 2H), 1.59 (quint., J = 7.4 Hz, 2H), 1.33 (sext., J = 7.4 Hz, 2H), 0.87 ppm (t, J = 7.4 Hz, 3H).

2-*n*-Butyl-5-(4-(trifluoromethyl)phenyl)furan (3)[5b]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 4-trifluoromethylbenzenesulfonyl chloride (0.367 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 95:5) to afford the desired compound **3** in 90% (0.242 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, J = 8.6 Hz, 2H), 7.59 (d, J = 8.6 Hz, 2H), 6.67 (d, J = 3.2 Hz, 1H), 6.10 (d, J = 3.2 Hz, 1H), 2.70 (t, J = 7.4 Hz, 2H), 1.69 (quint., J = 7.4 Hz, 2H), 1.45 (sext., J = 7.4 Hz, 2H), 0.96 ppm (t, J = 7.4 Hz, 3H).

2-*n*-Butyl-5-(4-chlorophenyl)furan (4)[10b]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 4-chlorobenzenesulfonyl chloride (0.317 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 90:10) to afford the desired compound **4** in 64% (0.150 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, J = 8.6 Hz, 2H), 7.20 (d, J = 8.6 Hz, 2H), 6.42 (d, J = 3.2 Hz, 1H), 5.95 (d, J = 3.2 Hz, 1H), 2.58 (t, J = 7.4 Hz, 2H), 1.56 (quint., J = 7.4 Hz, 2H), 1.33 (sext., J = 7.4 Hz, 2H), 0.86 ppm (t, J = 7.4 Hz, 3H).

2-(4-Bromophenyl)-5-*n*-butylfuran (5)[10b]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.383 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 90:10) to afford the desired compound **5** in 89% (0.249 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, J = 8.6 Hz, 2H), 7.36 (d, J =

8.6 Hz, 2H), 6.44 (d, J=3.2 Hz, 1H), 5.95 (d, J=3.2 Hz, 1H), 2.57 (t, J=7.4 Hz, 2H), 1.56 (quint., J=7.4 Hz, 2H), 1.32 (sext., J=7.4 Hz, 2H), 0.86 ppm (t, J=7.4 Hz, 3H).

2-*n*-Butyl-5-(3-(trifluoromethyl)phenyl)furan (7)[10b]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 3-trifluoromethylbenzenesulfonyl chloride (0.367 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 98:2) to afford the desired compound **7** in 48% (0.129 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.77 (s, 1H), 7.69 (m, 1H), 7.40–7.33 (m, 2H), 6.54 (d, J=3.2 Hz, 1H), 6.00 (d, J=3.2 Hz, 1H), 2.61 (t, J=7.4 Hz, 2H), 1.60 (quint., J=7.4 Hz, 2H), 1.35 (sext., J=7.4 Hz, 2H), 0.88 ppm (t, J=7.4 Hz, 3H).

2-*n*-Butyl-5-(2-nitrophenyl)furan (8)

2-*n*-Butylfuran (0.124 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **8** in 81% (0.199 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.62 (d, J=8.0 Hz, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.46 (dt, J=1.4, 7.7 Hz, 1H), 7.27 (ddd, J=1.4 and 7.4 and 8.0 Hz, 1H), 6.51 (d, J=3.3 Hz, 1H), 6.02 (d, J=3.2 Hz, 1H), 2.58 (t, J=7.5 Hz, 2H), 1.57 (quint., J=7.5 Hz, 2H), 1.32 (sext., J=7.5 Hz, 2H), 0.87 ppm (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=158.5, 147.2, 146.4, 131.7, 128.3, 127.5, 124.4, 123.8, 110.6, 107.3, 30.1, 27.8, 22.2, 13.8 ppm; elemental analysis calcd (%) for $C_{14}H_{15}NO_3$ (245.28): C 68.56, H 6.16; found: C 68.22, H 6.29.

2-*n*-Butyl-5-(2,4-dinitrophenyl)furan (9)

2-*n*-Butylfuran (0.124 g, 1 mmol) and 2,4-dinitrobenzenesulfonyl chloride (0.398 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 65:35) to afford the desired compound **9** in 46% (0.133 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.38 (d, J=2.3 Hz, 1H), 8.28 (dd, J=2.3 and 8.8 Hz, 1H), 7.84 (d, J=8.7 Hz, 1H), 6.76 (d, J=3.5 Hz, 1H), 6.12 (d, J=3.2 Hz, 1H), 2.62 (t, J=7.5 Hz, 2H), 1.60–1.54 (m, 2H), 1.39–1.26 (m, 2H), 0.88 ppm (t, J=7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=161.2, 145.7, 145.2, 144.3, 128.9, 128.0, 126.0, 119.7, 114.8, 108.7, 29.9, 27.7, 22.2, 13.6 ppm; elemental analysis calcd (%) for $C_{14}H_{14}N_2O_5$ (290.28): C 57.93, H 4.86; found: C 58.11, H 4.75.

2-*n*-Butyl-5-naphthalen-1-ylfuran (10)[31]

2-*n*-Butylfuran (0.124 g, 1 mmol) and 1-naphthalenesulfonyl chloride (0.340 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 90:10) to afford the desired compound **10** in 55% (0.138 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.46 (d, J=8.2 Hz, 1H), 7.88 (d, J=8.1 Hz, 1H), 7.80 (d, J=8.2 Hz, 1H), 7.72 (d, J=8.2 Hz, 1H), 7.55–7.45 (m, 3H), 6.63 (d, J=3.2 Hz, 1H), 6.18 (d, J=3.2 Hz, 1H), 2.77 (t, J=7.4 Hz, 3H), 1.76 (quint., J=7.4 Hz, 2H), 1.48 (sext., J=7.4 Hz, 2H), 0.98 ppm (t, J=7.4 Hz, 3H).

2-(4-Cyanophenyl)-3,6-dimethyl-4,5,6,7-tetrahydrobenzofuran (11)[5b]

Menthofuran (0.150 g, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.303 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **11** in 82% (0.205 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.57 (d, J=8.6 Hz, 2H), 7.52(d, J=8.6 Hz, 2H), 2.70–2.60 (m, 1H), 2.40–2.10 (m, 3H), 2.10 (s, 3H), 1.90–1.70 (m, 2H), 1.40–1.10 (m, 1H), 1.02 ppm (d, J=7.5 Hz, 3H).

3,6-Dimethyl-2-(2-nitrophenyl)-4,5,6,7-tetrahydrobenzofuran (12)

Menthofuran (0.150 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 75:25 to afford the desired compound **12** in 65% yield (0.176 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.73 (d, J=8.1 Hz, 1H), 7.50 (t, J=7.3 Hz, 1H), 7.44 (dd, J=1.8 and 7.7 Hz, 1H), 7.31 (dt, J=1.6 and 7.7 Hz, 1H), 2.60 (ddd, J=1.5 and 5.1 and 16.5 Hz, 1H), 2.36–2.28 (m, 2H), 2,16–2.12 (m, 1H), 1.84 (s, 3H), 1.90–1.83 (m, 1H), 1.81–1.75 (m, 1H), 1.37–1.27 (m, 1H), 1.01 ppm (d, J=6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=151.7, 148.1, 142.2, 132.0, 130.3, 127.5, 125.9, 124.5, 119.5, 119.2, 31.3, 31.1, 29.6, 21.5, 20.1, 9.2 ppm; elemental analysis calcd (%) for $C_{16}H_{17}NO_3$ (271.32): C 70.83, H 6.32; found: C 70.75, H 6.21.

2-Methyl-5-(4-nitrophenyl)furan (13)[32]

2-Methylfuran (177 μL, 2 mmol) and 4-nitrobenzenesulfonyl chloride (0.221 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 75:25) to afford the desired compound **13** in 67% (0.136 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.22 (d, J=8.2 Hz, 2H), 7.73 (d, J=8.2 Hz, 2H), 6.78 (d, J=3.0 Hz, 1H), 6.14 (d, J=3.0 Hz, 1H), 2.41 ppm (s, 3H).

2-(4-Cyanophenyl)-5-methylfuran (14)[33]

2-Methylfuran (177 μL, 2 mmol) and 4-cyanobenzenesulfonyl chloride (0.201 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **14** in 48% (0.088 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.61 (d, J=8.6 Hz, 2H), 7.55 (d, J=8.6 Hz, 2H), 6.63 (d, J=3.3 Hz, 1H), 6.08–6.02 (m, 1H), 2.32 ppm (s, 3H).

1-(5-(2-Nitrophenyl)furan-2-yl)propan-2-one (15)

1-(Furan-2-yl)propan-2-one (248 mg, 2 mmol) 2-nitrobenzenesulfonyl chloride (0.221 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **15** in 76% (0.186 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.70 (ddd, J=1.4 and 2.1 and 8.0 Hz, 2H), 7.59 (t, J=7.7 Hz, 1H), 7.42 (dd, J=7.4 and 8.1 Hz, 1H), 6.66 (d, J=3.4 Hz, 1H), 6.35 (d, J=3.3 Hz, 1H), 3.76 (s, 2H), 2.24 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=203.5, 150.0, 148.1, 147.4, 131.9, 128.8, 128.3, 124.0, 123.9, 110.9, 110.7, 43.3, 29.3 ppm; elemental analysis calcd (%) for $C_{13}H_{11}NO_4$ (245.23): C 63.67, H 4.52; found: C 63.95, H 4.21.

2-(4-Nitrophenyl)benzofuran (16)[34]

Benzofuran (0.118 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.331 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **16** in 83% (0.198 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.32 (d, J=7.8 Hz, 2H), 8.10 (d, J=7.8 Hz,

2H), 7.64 (d, J=8.0 Hz, 1H), 7.56 (d, J=8.0 Hz, 1H), 7.37 (t, J=7.8 Hz, 1H), 7.29 (t, J=7.8 Hz, 1H), 7.26 ppm (s, 1H).

2-(4-Methoxyphenyl)benzofuran (17)[34]

Benzofuran (0.118 g, 1 mmol) and 4-methoxybenzenesulfonyl chloride (0.310 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **17** in 38% (0.085 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.82 (d, J=7.8 Hz, 2H), 7.58 (d, J=8.0 Hz, 1H), 7.53 (d, J=8.0 Hz, 1H), 7.30 (t, J=7.8 Hz, 1H), 7.25 (t, J=7.8 Hz, 1H), 6.99 (d, J=7.8 Hz, 2H), 6.90 (s, 1H), 3.87 ppm (s, 3H).

2-(4-Bromophenyl)benzofuran (18)[35]

Benzofuran (0.118 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.384 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **18** in 79% (0.215 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.73 (d, J=7.8 Hz, 2H), 7.57 (d, J=8.0 Hz, 1H), 7.56 (d, J=7.8 Hz, 2H), 7.52 (d, J=8.0 Hz, 1H), 7.31 (t, J=7.8 Hz, 1H), 7.25 (t, J=7.8 Hz, 1H), 7.02 ppm (s, 1H).

2-(2-Fluorophenyl)benzofuran (19)[36]

Benzofuran (0.118 g, 1 mmol) and 2-fluorobenzenesulfonyl chloride (0.291 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 95:5) to afford the desired compound **19** in 84% (0.178 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.07 (t, J=7.7 Hz, 1H), 7.64 (d, J=7.7 Hz, 1H), 7.57 (d, J=8.0 Hz, 1H), 7.68–7.24 (m, 5H), 7.19 ppm (dd, J=8.6 and 8.0 Hz, 1H).

2-(2-Nitrophenyl)benzofuran (20)[37]

Benzofuran (0.118 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **20** in 52% (0.124 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.79 (d, J=8.0 Hz, 1H), 7.73 (d, J=8.4 Hz, 1H), 7.61 (d, J=8.0 Hz, 1H), 7.58–7.47 (m, 2H), 7.42 (t, J=7.6 Hz, 1H), 7.34 (t, J=7.6 Hz, 1H), 7.27 (t, J=7.2 Hz, 1H), 7.01 ppm (s, 1H).

1-Methyl-2-(4-nitrophenyl)pyrrole (21)[12]

1-Methylpyrrole (0.162 g, 2 mmol) and 4-nitrobenzenesulfonyl chloride (0.222 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **21** in 92% (0.186 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.18 (d, J=8.6 Hz, 2H), 7.48 (d, J=8.6 Hz, 2H), 6.74 (m, 1H), 6.34 (dd, J=1.7 and 3.4 Hz, 1H), 6.18 (t, J=3.4 Hz, 1H), 3.68 ppm (s, 3H).

1-Methyl-2-(4-cyanophenyl)pyrrole (22)[12]

1-Methylpyrrole (0.162 g, 2 mmol) and 4-cyanobenzenesulfonyl chloride (0.202 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **22** in 89% (0.162 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.60 (d, J=8.6 Hz, 2H), 7.43 (d, J=8.6 Hz, 2H), 6.71 (m, 1H), 6.28 (dd, J=3.4, 1.7 Hz, 1H), 6.16 (t, J=3.4 Hz, 1H), 3.64 ppm (s, 3H).

1-Methyl-2-(4-methoxyphenyl)pyrrole (23)[12]

1-Methylpyrrole (0.162 g, 2 mmol) and 4-methoxybenzenesulfonyl chloride (0.207 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **23** in 48% (0.090 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.24 (d, J=8.6 Hz, 2H), 6.85 (d, J=8.6 Hz, 2H), 6.61 (m, 1H), 6.10 (t, J=3.4 Hz, 1H), 6.07 (dd, J=3.4, 1.7 Hz, 1H), 3.76 (s, 3H), 3.54 ppm (s, 3H).

2-(4-Bromophenyl)-1-methylpyrrole (24)[38]

1-Methylpyrrole (0.162 g, 2 mmol) and 4-bromobenzenesulfonyl chloride (0.255 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **24** in 75% (0.177 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.51 (d, J=6.8 Hz, 2H), 7.26 (d, J=6.4 Hz, 2H), 6.73–6.71 (m, 1H), 6.24–6.21 (dd, J=1.8 and 3.4 Hz, 1H), 6.20 (t, J=3.4 Hz, 1H), 3.66 ppm (s, 3H).

1-Methyl-2-(2-nitrophenyl)pyrrole (25)[5e]

1-Methylpyrrole (0.162 g, 2 mmol) and 2-nitrobenzenesulfonyl chloride (0.222 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **25** in 86% (0.173 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.85 (d, J=8.6 Hz, 1H), 7.54 (t, J=8.0 Hz, 1H), 7.42 (t, J=8.0 Hz, 1H), 7.38 (d, J=8.6 Hz, 1H), 6.67 (m, 1H), 6.12 (t, J=3.4 Hz, 1H), 6.06 (dd, J=1.7 and 3.4 Hz, 1H), 3.36 ppm (s, 3H).

1-Benzyl-2-(4-nitrophenyl)pyrrole (26)[12]

1-Benzylepyrrole (0.314 g, 2 mmol) and 4-nitrobenzenesulfonyl chloride (0.222 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **26** in 87% (0.242 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=d 8.07 (d, J=8.7 Hz, 2H), 7.36 (d, J=8.7 Hz, 2H), 7.25–7.15 (m, 3H), 6.92 (dd, J=1.6 and 7.4 Hz, 2H), 6.78 (dd, J=1.8 and 2.7 Hz, 1H), 6.37 (dd, J=1.7 and 3.6 Hz, 1H), 6.24 (dd, J=2.7 and 3.7 Hz, 1H), 5.12 ppm (s, 2H).

2-(4-Nitrophenyl)-1-phenylpyrrole (27)[5e]

1-Phenylpyrrole (0.286 g, 2 mmol) and 4-nitrobenzenesulfonyl chloride (0.222 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **27** in 63% (0.166 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.98 (d, J=8.6 Hz, 2H), 7.32–7.25 (m, 3H), 7.16 (d, J=8.6 Hz, 2H), 7.10 (d, J=8.6 Hz, 2H), 6.95 (s, 1H), 6.56 (dd, J=1.7 and 3.4 Hz, 1H), 6.34 ppm (t, J=3.4 Hz, 1H).

2-(2-Nitrophenyl)-1-phenylpyrrole (28)

1-Phenylpyrrole (0.286 g, 2 mmol) and 2-nitrobenzenesulfonyl chloride (0.222 g, 1 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **28** in 73% (0.192 g) yield. ^{1}H NMR

(400 MHz, $CDCl_3$): $\delta = 7.63$ (dd, $J = 1.5$ and 8.5 Hz, 1H), 7.41 (dt, $J = 1.4$ and 7.4 Hz, 1H), 7.29 (d, $J = 8.0$ Hz, 2H), 7.21–7.14 (m, 3H), 7.00 (dd, $J = 2.0$ and 8.3 Hz, 2H), 6.94 (t, $J = 2.3$ Hz, 1H), 6.32 ppm (d, $J = 2.3$ Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 149.2$, 139.5, 133.0, 132.3, 129.3, 128.2, 128.1, 128.0, 126.9, 125.3, 124.5, 124.2, 111.9, 109.8 ppm; elemental analysis calcd (%) for $C_{16}H_{12}N_2O_2$ (264.28): C 72.72, H 4.58; found: C 72.91, H 4.37.

2-(4-Bromophenyl)-1-methylindole (29a)[39]

1-Methylindole (0.196 g, 1.5 mmol) and 4-bromobenzenesulfonyl chloride (0.255 g, 1 mmol) without solvent, the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **29a** in 62% (0.177 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.73$ (d, $J = 7.8$ Hz, 1H), 7.70–7.65 (m, 2H), 7.48–7.42 (m, 3H), 7.38–7.32 (m, 1H), 7.27–7.21 (m, 1H), 6.64 (d, $J = 0.7$ Hz, 1H), 3.81 ppm (s, 3H).

3-(4-Bromophenyl)-1-methylindole (29b)[40]

Methylindole (0.196 g, 1.5 mmol) and 4-bromobenzenesulfonyl chloride (0.255 g, 1 mmol) in DEC, the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **29b** in 29% (0.083 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.89$ (d, $J = 8.0$ Hz, 1H), 7.50–7.57 (m, 4H), 7.37 (d, $J = 8.2$ Hz, 1H), 7.30 (dt, $J = 1.0$ and 7.6 Hz, 1H), 7.22 (s, 1H), 7.21 (dt, $J = 1.0$ and 7.5 Hz, 1H), 3.83 ppm (s, 3H).

2-(2-Bromophenyl)-1-methylindole (30a)[41]

Methylindole (0.196 g, 1.5 mmol) and 2-bromobenzenesulfonyl chloride (0.255 g, 1 mmol) without solvent, the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **30a** in 71% (0.203 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.70$–7.75 (m, 2H), 7.20–7.45 (m, 6H), 6.56 (s, 1H), 3.61 ppm (s, 3H).

4-(4-Nitrophenyl)-2-*n*-pentylthiophene (31)

2-*n*-Pentylthiophene (163 μL, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **31** in 80% (0.220 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.26$ (d, $J = 8.7$ Hz, 2H), 7.72 (d, $J = 8.7$ Hz, 2H), 7.44 (d, $J = 1.8$ Hz, 1H), 7.13 (d, $J = 1.8$ Hz, 1H), 2.88 (t, $J = 7.6$ Hz, 2H), 1.78–1.70 (m, 2H), 1.42–1.38 (m, 4H), 0.94 ppm (t, $J = 6.86$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 148.0$, 146.5, 142.3, 139.4, 126.6, 124.3, 122.9, 120.8, 31.3, 30.2, 27.0, 22.4, 14.0 ppm; elemental analysis calcd (%) for $C_{15}H_{17}NO_2S$ (275.37): C 65.43, H 6.22; found: C 65.21, H 6.59.

4-(4-Cyanophenyl)-2-*n*-pentylthiophene (32)

2-*n*-Pentylthiophene (163 μL, 1 mmol) and 4-cyanobenzenesulfonyl chloride (0.302 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 75:25) to afford the desired compound **32** in 84% (0.215 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.65$ (brs, 4H), 7.35 (d, $J = 1.5$ Hz, 1H), 7.08 (d, $J = 1.5$ Hz, 1H), 2.84 (t, $J = 7.5$ Hz, 2H), 1.72 (quint, $J = 7.1$ Hz, 2H), 1.41–1.33 (m, 4H), 0.92 ppm (t, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.9$, 140.6, 140.0, 132.9, 126.9, 123.1, 120.5, 119.3, 110.4, 77.5, 31.5, 30.4, 22.7, 14.3 ppm; elemental analysis calcd (%) for $C_{16}H_{17}NS$ (255.38): C 75.25, H 6.71; found: C 75.41, H 7.02.

4-(4-Bromophenyl)-2-*n*-pentylthiophene (33)

2-*n*-Pentylthiophene (163 μL, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.255 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **33** in 74% (0.229 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.52$ (d, $J = 8.0$ Hz, 2H), 7.46 (d, $J = 8.0$ Hz, 2H), 7.24 (d, $J = 1.7$ Hz, 1H), 7.06 (brs, 1H), 2.86 (t, $J = 7.5$ Hz, 2H), 1.79–1.69 (m, 2H), 1.45–1.36 (m, 4H), 0.96 ppm (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.2$, 140.6, 135.2, 131.8, 127.8, 123.1, 120.8, 118.2, 31.4, 30.3, 30.2, 22.5, 14.1 ppm; elemental analysis calcd (%) for $C_{15}H_{17}BrS$ (309.27): C 58.26, H 5.54; found: C 58.45, H 5.21.

4-(4-chlorophenyl)-2-*n*-pentylthiophene (34)

2-*n*-Pentylthiophene (163 μL, 1 mmol) and 4-chlorobenzenesulfonyl chloride (0.316 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **34** in 76% (0.201 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.51$ (d, $J = 8.5$ Hz, 2H), 7.35 (d, $J = 8.5$ Hz, 2H), 7.22 (d, $J = 1.6$ Hz, 1H), 7.05 (d, $J = 1.6$ Hz, 1H), 2.85 (t, $J = 7.6$ Hz, 2H), 1.79–1.67 (m, 2H), 1.43–1.35 (m, 2H), 0.93 ppm (t, $J = 6.1$ Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.4$, 140.8, 135.0, 132.9, 129.1, 127.7, 123.4, 118.3, 31.5, 30.4, 29.9, 22.6, 14.2 ppm; elemental analysis calcd (%) for $C_{15}H_{17}ClS$ (264.81): C 68.04, H 6.47; found: C 68.31, H 6.68.

2-Methyl-4-(4-nitrophenyl)thiophene (36)[11]

2-Methylthiophene (97 μL, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **36** in 89% (0.195 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.22$ (d, $J = 8.8$ Hz, 2H), 7.68 (d, $J = 8.8$ Hz, 2H), 7.38 (s, 1H), 7.10 (s, 1H), 2.55 ppm (s, 3H).

4-(4-Bromophenyl)-2-methylthiophene (37)[11]

2-Methylthiophene (97 μL, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.383 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **37** in 40% (0.101 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.49$ (d, $J = 8.2$ Hz, 2H), 7.41 (d, $J = 8.2$ Hz, 2H), 7.18 (s, 1H), 7.02 (s, 1H), 2.53 ppm (s, 3H).

4-(4-Chlorophenyl)-2-methylthiophene (38)[11]

2-Methylthiophene (97 μL, 1 mmol) and 4-chlorobenzenesulfonyl chloride (0.316 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 80:20) to afford the desired compound **38** in 73% (0.152 g) yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.48$ (d, $J = 8.0$ Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 7.18 (s, 1H), 7.02 (s, 1H), 2.53 ppm (s, 3H).

4-(4-Nitrophenyl)-2,2′-bithiophene (39)

2,2′-Bithiophene (0.166 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **39** in 66% (0.190 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (d, J = 9.0 Hz, 2H), 7.68 (d, J = 8.8 Hz, 2H), 7.42 (dd, J = 1.6 and 8.2 Hz, 2H), 7.23–7.17 (m, 2H), 6.99 ppm (dd, J = 3.6 and 5.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 136.5, 141.6, 139.3, 127.9, 126.7, 125.1, 124.3, 122.3, 121.8 ppm; elemental analysis calcd (%) for $C_{14}H_9NO_2S_2$ (287.35): C 58.52, H 3.16; found: C 58.88, H 3.31.

3-Chloro-4-(4-nitrophenyl)thiophene (40)

3-Methylthiophene (0.119 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **40** in 35% (0.084 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, J = 8.7 Hz, 2H), 7.73 (d, J = 8.7 Hz, 2H), 7.46 (d, J = 3.6 Hz, 1H), 7.35 ppm (d, J = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.6, 141.0, 138.3, 129.7, 125.4, 124.7, 123.9, 122.6 ppm; elemental analysis calcd (%) for $C_{10}H_6ClNO_2S$ (264.81): C 50.11, H 2.52; found: C 50.41, H 2.36.

3-Methyl-4-(4-nitrophenyl)thiophene (41)

3-Methylthiophene (0.098 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **41** in 79% (0.173 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (d, J = 8.9 Hz, 2H), 7.58 (d, J = 8.7 Hz, 2H), 7.35 (d, J = 3.4 Hz, 1H), 7.11 (d, J = 2.7 Hz, 1H), 2.32 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.8, 143.7, 140.8, 135.7, 129.2, 124.9, 123.7, 123.3, 15.6 ppm; elemental analysis calcd (%) for $C_{11}H_9NO_2S$ (219.26): C 60.26, H 4.14; found: C 60.56, H 4.33.

2-Bromo-4-(4-nitrophenyl)-3-methylthiophene (42)

2-Bromo-3-methylthiophene (0.177 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **42** in 56% (0.177 g). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.6 Hz, 2H), 7.43 (d, J = 8.6 Hz, 2H), 7.19 (s, 1H), 2.12 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.1, 143.3, 140.8, 135.2, 129.3, 124.1, 123.8, 111.9, 14.9 ppm; elemental analysis calcd (%) for $C_{11}H_8BrNO_2S$ (298.15): C 44.31, H 2.70; found: C 44.76, H 3.01.

3-(4-Nitrophenyl)benzothiophene (43)

Benzothiophene (0.134 g, 1 mmol) and 4-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **43** in 85% (0.217 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, J = 8.7 Hz, 2H), 7.88–7.84 (m, 1H), 7.81–7.77 (m, 1H), 7.66 (d, J = 8.7 Hz, 2H), 7.46 (s, 1H), 7.38–7.33 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.1, 142.6, 140.8, 137.0, 135.8, 129.3, 125.8, 125.0, 125.0, 124.1, 123.2, 122.4 ppm; elemental analysis calcd (%) for $C_{14}H_9NO_2S$ (255.29): C 65.87, H 3.55; found: C 66.09, H 3.28.

3-(4-Bromophenyl)benzothiophene (44)[11]

Benzothiophene (0.134 g, 1 mmol) and 4-bromobenzenesulfonyl chloride (0.383 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 85:15) to afford the desired compound **44** in 88% (0.253 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96–7.84 (m, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.42–7.39 ppm (m, 3H).

3-(2-Nitrophenyl)benzothiophene (45)

Benzothiophene (0.134 g, 1 mmol) and 2-nitrobenzenesulfonyl chloride (0.332 g, 1.5 mmol) were used, and the residue was purified by flash chromatography on silica gel (heptane/ethyl acetate, 70:30) to afford the desired compound **45** in 85% (0.217 g) yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.74 (m, 2H), 7.73–7.70 (m, 1H), 7.59–7.54 (m, 2H), 7.48–7.43 (m, 1H), 7.32–7.28 (m, 2H), 7.19 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.4, 139.9, 139.3, 137.4, 132.5, 132.1, 129.2, 128.6, 124.9, 124.7, 124.1, 124.0, 123.8, 122.2 ppm; elemental analysis calcd (%) for $C_{14}H_9NO_2S$ (255.29): C 65.87, H 3.55; found: C 65.98, H 3.41.

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