JOC The Journal of Organic Chemistry

NOTE

pubs.acs.org/joc

Palladium-Catalyzed Direct Arylation of Thiophenes Bearing SO_2R Substituents

Charles Beromeo Bheeter,[†] Jitendra K. Bera,[‡] and Henri Doucet[†,*]

[†]Institut Sciences Chimiques de Rennes, UMR 6226 CNRS, Université de Rennes "Catalyse et Organometalliques", Campus de Beaulieu, 35042 Rennes, France

[‡]Department of Chemistry, Indian Institute of Technology Kanpur, 208016 Kanpur, India

Supporting Information

ABSTRACT: The palladium-catalyzed direct arylation of SO_2R-substituted thiophene derivatives was found to proceed regioselectively at C5 and in high yields using a variety of aryl bromides and as low as 0.5−0.1 mol % of phosphine-free $Pd(OAc)_2$ as the catalyst. For these reactions, sulfonyls, sulfonamides, or even a sulfonic ester as the thiophene substituents were successfully employed.

The palladium-catalyzed direct arylation of several heteroaromatics via a C−H bond activation using aryl halides has led to successes in recent years.[1−4] However, there are still limitations for these reactions in terms of heteroaromatic functional group tolerance. The presence of acetyl, formyl, nitrile, hydroxyalkyl, amino, or silyl as the functional groups on the thiophenes for palladium-catalyzed arylation has been described.[5] A direct arylation of a furan substituted by a methyl sulfide in the presence of an iridium catalyst has also been reported.[6] On the other hand, to our knowledge, direct arylations in the presence of heteroaromatics bearing sulfonyls, sulfonamides, or sulfonic esters as the substituents has not been described, although they are very common groups in bioactive molecules (Figure 1).

Arylated SO_2R-substituted thiophenes can be prepared by Suzuki coupling using halothiophenes with arylboronic acids[7] or by reaction of arylthiophenes with sulfuric acid.[8] However, Suzuki coupling requires the preparation of an arylboronic acid and provides an organometallic salt (MX) as byproduct, and the use of sulfuric acid requires very stable reactants. Therefore, the direct arylation of thiophenes bearing SO_2R functions via a C−H bond activation would be very convenient since it would provide a more environmentally and economically attractive access to such arylated thiophenes.

Here, we wish to report on the reaction of thiophene derivatives bearing sulfonyls, sulfonamides, or sulfonic esters as substituents with a set of electronically and sterically diverse aryl bromides in the presence of a low loading of a phosphine-free palladium catalyst.

We decided to employ commercially available 2-methanesulfonylthiophene and 4-bromobenzonitrile as the test substrates for our study (Table 1). We initially examined the influence of the nature of the base on the product distribution for this reaction using DMAc as the solvent and $PdCl(C_3H_5)(dppb)$ as the catalyst. This palladium complex was recently demonstrated to be one of the best catalyst for the direct arylation of some furans, thiophenes, or thiazoles.[5g,5o] K_2CO_3 or Na_2CO_3 gave poor conversions of 4-bromobenzonitrile, and the target compound **1** was obtained in low yields (Table 1, entries 1 and 2). The use of acetates such as NaOAc, KOAc, or CsOAc as base gave better results, as complete conversions of 4-bromobenzonitrile were obseved in the presence of 0.5 mol % of catalyst (Table 1, entries 3−5). The good performance of acetates as the base is consistent with a concerted metalation deprotonation (CMD) pathway.[9] Then, we performed reactions using 0.1 mol % catalyst. CsOAc or NaOAc led to partial conversions of 4-bromobenzonitrile, whereas a complete conversion was observed in the presence of KOAc (Table 1, entries 6−8). The nature of the solvent often modifies the catalyst activity in cross-coupling reactions; thus we observed that NMP and DMF in the presence of 0.1 mol % of $PdCl(C_3H_5)(dppb)$ as the catalyst also gave **1** in moderate yields (Table 1, entries 9 and 10). We then evaluated the influence of the palladium source. Interestingly, 0.5 mol % of $Pd(OAc)_2$ gave **1** very selectively (Table 1, entry 11). Moreover, the use of only 0.1 mol % of $Pd(OAc)_2$ gave **1** in 100% conversion and in 82% yield (Table 1, entry 12). This phosphine-free catalyst had already been found to be very efficient for the direct arylation of other thiophene derivatives.[5h]

Then, 2-methanesulfonylthiophene was coupled with three other aryl bromides in the presence of 0.1 mol % of $Pd(OAc)_2$ and KOAc as the base (Table 2). Selective 5-arylations were observed using 4-bromoacetophenone, 4-bromobenzaldehyde, or 2-bromobenzonitrile, resulting in 71−74% yields of the products **2**−**4**.

Very similar results were obtained in the presence of an isopropyl instead of a methyl substituent on the sulfonyl group (Table 3). A wide range of aryl bromides was employed, and in all cases, the expected 5-arylated thiophenes were selectively obtained using 0.5−0.1 mol % of $Pd(OAc)_2$ as the catalyst and KOAc as the base. The reaction of methyl 4-bromobenzoate or

Received: May 9, 2011
Published: June 22, 2011

ACS Publications © 2011 American Chemical Society

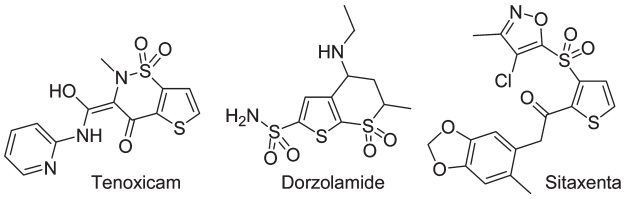
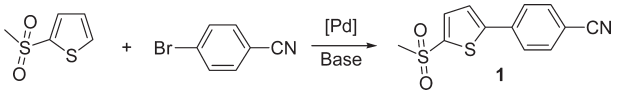


Figure 1. Examples of bioactive thiophenes bearing SO_2R substituents.

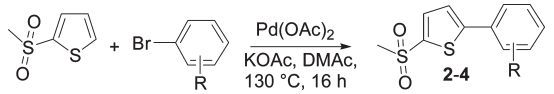
Table 1. Influence of the Reaction Conditions on the Arylation of 2-Methanesulfonylthiophene with 4-Bromobenzonitrile[a]



entry	solvent	base	catalyst (mol %)	convn (%)
1	DMAc	K_2CO_3	$PdCl(C_3H_5)(dppb)$ (0.5)	25
2	DMAc	Na_2CO_3	$PdCl(C_3H_5)(dppb)$ (0.5)	42
3	DMAc	CsOAc	$PdCl(C_3H_5)(dppb)$ (0.5)	100
4	DMAc	NaOAc	$PdCl(C_3H_5)(dppb)$ (0.5)	100
5	DMAc	KOAc	$PdCl(C_3H_5)(dppb)$ (0.5)	100
6	DMAc	CsOAc	$PdCl(C_3H_5)(dppb)$ (0.1)	51
7	DMAc	NaOAc	$PdCl(C_3H_5)(dppb)$ (0.1)	32
8	DMAc	KOAc	$PdCl(C_3H_5)(dppb)$ (0.1)	100 (80)
9	NMP	KOAc	$PdCl(C_3H_5)(dppb)$ (0.1)	62
10	DMF	KOAc	$PdCl(C_3H_5)(dppb)$ (0.1)	70
11	DMAc	KOAc	$Pd(OAc)_2$ (0.5)	100
12	DMAc	KOAc	$Pd(OAc)_2$ (0.1)	100 (82)

[a] Conditions: [Pd], 4-bromobenzonitrile (1 equiv), 2-methanesulfonylthiophene (1.5 equiv), base (2 equiv), 16 h, 130 °C, conversion of 4-bromobenzonitrile, isolated yields of **1** in parentheses.

Table 2. Direct Arylation of 2-Methanesulfonylthiophene[a]

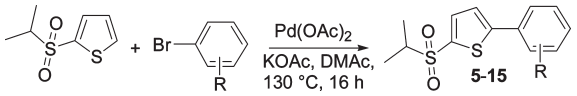


entry	R	product	yield (%)
1	4-COMe	**2**	73
2	4-CHO	**3**	74
3	2-CN	**4**	71

[a] Conditions: $Pd(OAc)_2$ (0.001 equiv), aryl bromide (1 equiv), 2-methanesulfonylthiophene (1.5 equiv), KOAc (2 equiv), 16 h, 130 °C.

4-bromonitrobenzene gave products **5** and **6** in 67% and 61% yields, respectively. It should be noted that even 4-chlorobromobenzene could be employed to give **7** in 73% yield. In the course of this reaction, no cleavage of the C−Cl bond was observed, allowing further transformations. 4-Fluorobromobenzene was also successfully coupled with 2-(propane-2-sulfonyl)-thiophene to give **8** in 75% yield. The reaction of electron-rich aryl bromide, 4-*tert*-butylbromobenzene, led to **9** in a slightly lower yield of 56% when 0.1 mol % catalyst was employed due to a partial conversion of this aryl bromide. In the presence of 0.5 mol % of $Pd(OAc)_2$, a complete conversion of this aryl

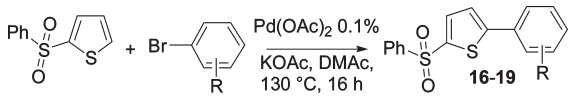
Table 3. Direct Arylation of 2-(Propane-2-sulfonyl)-thiophene[a]



entry	R or aryl bromide	product	yield (%)
1	4-CO_2Me	**5**	67[b]
2	4-NO_2	**6**	61
3	4-Cl	**7**	73
4	4-F	**8**	75
5	4-*t*-Bu	**9**	70[b]
6	3-COMe	**10**	72
7	2-CN	**11**	78
8	1-bromonaphthalene	**12**	77
9	5-bromopyrimidine	**13**	91
10	4-bromoisoquinoline	**14**	72
11	4-bromopyridine hydrochloride	**15**	68

[a] Conditions: $Pd(OAc)_2$ (0.001 equiv.), aryl bromide (1 equiv), 2-(propane-2-sulfonyl)thiophene (1.5 equiv), KOAc (2 equiv), 16 h, 130 °C. [b] $Pd(OAc)_2$ (0.005 equiv).

Table 4. Direct Arylation of 2-Benzenesulfonylthiophene[a]



entry	R	product	yield (%)
1	4-CHO	**16**	72
2	4-CN	**17**	71
3	4-CO_2Me	**18**	73
4	2-CN	**19**	76

[a] Conditions: $Pd(OAc)_2$ (0.001 equiv), aryl bromide (1 equiv), 2-benzenesulfonylthiophene (1.5 equiv), KOAc (2 equiv), 16 h, 130 °C.

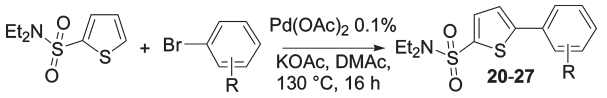
bromide was observed and a yield of 70% in **9** was obtained. The *meta*-substituted aryl bromide, 3-bromoacetophenone, gave **10** in 72% yield. More congested substrates, such as 2-bromobenzonitrile or 1-bromonaphthalene, were also found to be suitable coupling partners and gave **11** and **12** in 78% and 77% yields, respectively. On the other hand, chlorobenzene and the electron-rich aryl bromide 4-bromoanisole were found to be unreactive. We observed that the coupling of 4-bromopyridine, 4-bromoisoquinoline, or 5-bromopyrimidine with 2-(propane-2-sulfonyl)-thiophene also proceed nicely to give **13**−**15** in 68−91% yields.

Again, similar results were obtained for the coupling with of 2-benzenesulfonylthiophene (Table 4). In the presence of 2- or 4-bromobenzonitriles, 4-bromobenzaldehyde or methyl 4-bromobenzoate and 0.1 mol % $Pd(OAc)_2$, the products **16**−**19** were obtained in 71−76% yields. It should be noted that a regioselective arylation at carbon 5 of thiophene was observed and that no trace of arylation on the benzene ring was detected.

Then, we performed several reactions using thiophene-2-sulfonic acid diethylamide as the coupling partner (Table 5). The target products **20**−**27** were obtained in 75−87% yields using only 0.1 mol % of $Pd(OAc)_2$ as the catalyst at 130 °C as the reaction temperature. In all cases, the reactions were found

dx.doi.org/10.1021/jo200918n |*J. Org. Chem.* 2011, 76, 6407–6413

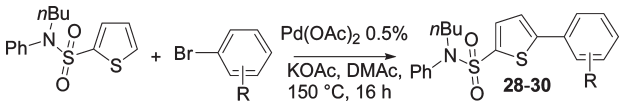
Table 5. Direct Arylation of Thiophene-2-sulfonic Acid Diethylamide[a]



entry	R or aryl bromide	poduct	yield (%)
1	4-CN	**20**	79
2	4-CHO	**21**	87
3	4-CO_2Me	**22**	80
4	4-COMe	**23**	75
5	4-COPh	**24**	81
6	2-CN	**25**	79
7	4-bromopyridine hydrochloride	**26**	91
8	4-bromoisoquinoline	**27**	86

[a] Conditions: $Pd(OAc)_2$ (0.001 equiv), aryl bromide (1 equiv), thiophene-2-sulfonic acid diethylamide (1.5 equiv), KOAc (2 equiv), 16 h, 130 °C.

Table 6. Direct Arylation of Thiophene-2-sulfonic Acid *n*-Butylphenylamide[a]



entry	R or aryl bromide	product	yield (%)
1	4-CN	**28**	75
2	1-bromonaphthalene	**29**	82
3	3-bromopyridine	**30**	76

[a] Conditions: $Pd(OAc)_2$ (0.005 equiv.), aryl bromide (1 equiv), thiophene-2-sulfonic acid *n*-butylphenylamide (1.5 equiv), KOAc (2 equiv), 16 h, 150 °C.

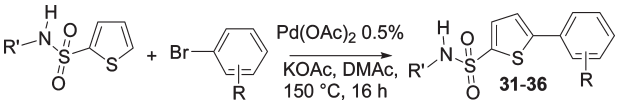
to be very clean, as only the arylation at C5 of thiophene was detected.

The reaction is not limited to the use of sulfonic acid dialkylamides. The reaction of 4-bromobenzonitrile, 1-bromonaphthalene, or 3-bromopyridine with thiophene-2-sulfonic acid *n*-butylphenylamide was also found to give very cleanly the direct arylation products **28**−**30** in 75−82% yields (Table 6). However, with this thiophene derivative, we had to employ a more elevated reaction temperature of 150 °C and a higher catalyst loading of 0.5 mol % in order to reach complete conversions of the aryl bromides.

Thiophene-2-sulfonic acid benzylamide was also found to be less reactive than 2-sulfonic acid diethylamide. At 130 °C, using 0.1 mol % of $Pd(OAc)_2$ as the catalyst, a moderate conversion of 4-bromobenzonitrile was observed. The presence of a free NH on this reactant might partially poison the catalyst. Again, we had to employ a reaction temperature of 150 °C and 0.5 mol % of catalyst loading of in order to obtain full conversions of the aryl bromides (Table 7). Using these conditions, the reaction of 2- or 4-bromobenzonitriles, 4-bromoacetophenone, or 4-bromopyridine gave **31**−**34** in 66−74% yields.

Thiophene-2-sulfonic acid phenylamide has also a lower reactivity than thiophene-2-sulfonic acid diethylamide, and the reactions had to be performed at 150 °C with 0.5 mol % of

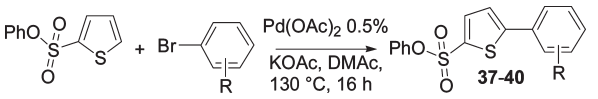
Table 7. Direct Arylation of Thiophene-2-sulfonic Acid Benzylamide or Thiophene-2-sulfonic Acid Phenylamide[a]



entry	R or aryl bromide	R′	product	yield (%)
1	4-CN	CH_2Ph	**31**	71
2	4-COMe	CH_2Ph	**32**	66
3	2-CN	CH_2Ph	**33**	74
4	4-bromopyridine hydrochloride	CH_2Ph	**34**	73
5	4-CN	Ph	**35**	61
6	4-NO2	Ph	**36**	60

[a] Conditions: $Pd(OAc)_2$ (0.005 equiv), aryl bromide (1 equiv), thiophene-2-sulfonic acid benzylamide or thiophene-2-sulfonic acid phenylamide (1.5 equiv), KOAc (2 equiv), 16 h, 150 °C.

Table 8. Direct Arylation of Thiophene-2-sulfonic Acid Phenyl Ester[a]



entry	R or aryl bromide	product	yield (%)
1	4-CN	**37**	72
2	2-CN	**38**	76
3	3-COMe	**39**	75
4	4-bromoisoquinoline	**40**	83

[a] Conditions: $Pd(OAc)_2$ (0.005 equiv), aryl bromide (1 equiv), thiophene-2-sulfonic acid phenyl ester (1.5 equiv), KOAc (2 equiv), 16 h, 130 °C.

catalyst. In the presence of 4-bromobenzonitrile or 4-bromonitrobenzene, the desired coupling products **35** and **36** were obtained in 61% and 60% yields, respectively (Table 7).

Finaly, the palladium-catalyzed reaction of four aryl bromides with thiophene-2-sulfonic acid phenyl ester has been examined (Table 8). The arylations using this substrate might give side products, as the palladium-catalyzed direct arylation of heteroaromatics using toylates or mesylates is possible in the presence of K_2CO_3/*t*-BuCO_2H.[10] However, the reaction of thiophene-2-sulfonic acid phenyl ester with 2- or 4-bromobenzonitriles, 3-bromoacetophenone, or 4-bromoisoquinoline gave cleanly **37**−**40** in 72−83% yield. In the course of these reactions no cleavage of the Ph−O bond was observed.

In summary, we report here conditions for the palladium-catalyzed regioselective direct arylation at C5 of a range of SO_2R-substituted thiophene derivatives. As low as 0.5−0.1 mol % of phosphine-free $Pd(OAc)_2$ as the catalyst associated to KOAc promotes the arylation of thiophenes bearing sulfonyls, sulfonamides, and even a sulfonic acid phenyl ester.

EXPERIMENTAL SECTION

General Procedure. As a typical experiment, the reaction of the aryl bromide (1 mmol), thiophene derivative (1.5 mmol), and KOAc (0.196 g, 2 mmol) at 130 or 150 °C (see Tables 1−8) during 16 h in

dx.doi.org/10.1021/jo200918n |*J. Org. Chem.* 2011, 76, 6407–6413

DMAc (4 mL) in the presence of $Pd(OAc)_2$ (0.224 mg, 0.001 mmol or 1.12 mg, 0.005 mmol, see tables) under argon affords the coupling product after addition of water (20 mL), extraction with dichloromethane (20 mL), drying on $MgSO_4$, evaporation, and purification on silica gel.

3-(5-Methanesulfonylthiophene-2-yl)benzonitrile (1). 4-Bromobenzonitrile (0.182 g, 1 mmol) and 2-methanesulfonylthiophene (0.243 g, 1.5 mmol) afford **1** in 82% (0.216 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.92 (d, J = 8.5 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H), 7.79 (d, J = 4.0 Hz, 1H), 7.67 (d, J = 4.0 Hz, 1H), 3.30 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 148.8, 142.7, 136.7, 135.0, 133.7, 127.3, 127.2, 118.9, 111.9, 45.7. Anal. Calcd for $C_{12}H_9NO_2S_2$ (263.34): C, 54.73; H, 3.44. Found: C, 54.89; H, 3.30.

1-[4-(5-Methanesulfonylthiophene-2-yl)-phenyl]ethanone (2). 4-Bromoacetophenone (0.199 g, 1 mmol) and 2-methanesulfonylthiophene (0.243 g, 1.5 mmol) afford **2** in 73% (0.204 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.03 (d, J = 8.4 Hz, 2H), 7.91 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 4.0 Hz, 1H), 7.81 (d, J = 4.0 Hz, 1H), 3.41 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 197.6, 149.7, 142.1, 137.3, 136.5, 135.0, 129.7, 126.7, 45.7, 27.2. Anal. Calcd for $C_{13}H_{12}O_3S_2$ (280.36): C, 55.69; H, 4.31. Found: C, 55.47; H, 4.50.

4-(5-Methanesulfonylthiophene-2-yl)benzaldehyde (3). 4-Bromobenzaldehyde (0.185 g, 1 mmol) and 2-methanesulfonylthiophene (0.243 g, 1.5 mmol) afford **3** in 74% (0.197 g) yield. ^{1}H NMR (300 MHz, DMSO-*d*6): δ 10.04 (s, 1H), 8.00 (s, 4H), 7.87 (d, J = 4.0 Hz, 1H), 7.85 (d, J = 4.0 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 192.9, 149.5, 142.5, 137.8, 136.7, 135.0, 130.9, 127.1, 127.0, 45.7. Anal. Calcd for $C_{12}H_{10}O_3S_2$ (266.34): C, 54.11; H, 3.78. Found: C, 54.21; H, 3.59.

2-(5-Methanesulfonylthiophene-2-yl)benzonitrile (4). 2-Bromobenzonitrile (0.182 g, 1 mmol) and 2-methanesulfonylthiophene (0.243 g, 1.5 mmol) afford **4** in 71% (0.187 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.02 (d, J = 7.7 Hz, 1H), 7.92 (d, J = 4.0 Hz, 1H), 7.85−7.80 (m, 2H), 7.71 (d, J = 4.0 Hz, 1H), 7.70−7.65 (m, 1H), 3.45 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 146.3, 143.5, 135.2, 135.1, 134.5, 134.3, 130.7, 130.3, 129.4, 118.5, 110.2, 45.7. Anal. Calcd for $C_{12}H_9NO_2S_2$ (263.34): C, 54.73; H, 3.44. Found: C, 54.84; H, 3.57.

Methyl 4-[5-(Propane-2-sulfonyl)thiophene-2-yl]benzoate (5). Methyl 4-bromobenzoate (0.215 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **5** in 67% (0.217 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.03 (d, J = 8.2 Hz, 2H), 7.94 (d, J = 8.2 Hz, 2H), 7.85 (d, J = 4.0 Hz, 1H), 7.81 (d, J = 4.0 Hz, 1H), 3.88 (s, 3H), 3.53 (sept, J = 7.5 Hz, 1H), 1.26 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 166.1, 150.7, 137.3, 136.8, 136.7, 130.6, 130.4, 126.8, 126.7, 56.3, 52.8, 16.0. Anal. Calcd for $C_{15}H_{16}O_4S_2$ (324.42): C, 55.53; H, 4.97. Found: C, 55.31; H, 4.80.

2-(4-Nitrophenyl)-5-(propane-2-sulfonyl)thiophene (6). 4-Bromonitrobenzene (0.202 g, 1 mmol) and 2-(propane-2-sulfonyl)-thiophene (0.285 g, 1.5 mmol) afford **6** in 61% (0.190 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.31 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 4.0 Hz, 1H), 7.50 (d, J = 4.0 Hz, 1H), 3.35 (sept, J = 7.5 Hz, 1H), 1.43 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.9, 147.9, 138.7, 138.5, 135.8, 126.9, 125.7, 124.6, 57.0, 16.0. Anal. Calcd for $C_{13}H_{13}NO_4S_2$ (311.38): C, 50.14; H, 4.21. Found: C, 50.01; H, 4.40.

2-(4-Chlorophenyl)-5-(propane-2-sulfonyl)thiophene (7). 4-Bromochlorobenzene (0.191 g, 1 mmol) and 2-(propane-2-sulfonyl)-thiophene (0.285 g, 1.5 mmol) afford **7** in 73% (0.219 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.81 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 4.0 Hz, 1H), 7.75 (d, J = 4.0 Hz, 1H), 7.54 (d, J = 8.5 Hz, 2H), 3.53 (sept, J = 7.5 Hz, 1H), 1.26 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 151.0, 136.8, 136.3, 134.5, 131.3, 129.8, 128.3, 125.8, 56.3, 16.0. Anal. Calcd for $C_{13}H_{13}ClO_2S_2$ (300.83): C, 51.90; H, 4.36. Found: C, 52.00; H, 4.44.

2-(4-Fluorophenyl)-5-(propane-2-sulfonyl)thiophene (8). 4-Bromofluorobenzene (0.175 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **8** in 75% (0.213 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.83 (dd, J = 8.6, 5.3 Hz, 2H), 7.75 (d, J = 4.0 Hz, 1H), 7.66 (d, J = 4.0 Hz, 1H), 7.32 (d, J = 8.6 Hz, 2H), 3.49 (sept, J = 7.5 Hz, 1H), 1.26 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 163.1 (d, J = 247.6 Hz), 151.3, 136.8, 135.8, 129.1 (d, J = 3.3 Hz), 128.9 (d, J = 8.5 Hz), 125.4, 116.8 (d, J = 22.0 Hz), 56.3, 16.0. Anal. Calcd for $C_{13}H_{13}FO_2S_2$ (284.37): C, 54.91; H, 4.61. Found: C, 54.87; H, 4.47.

2-(4-*tert*-Butylphenyl)-5-(propane-2-sulfonyl)thiophene (9). 4-*tert*-Butylbromobenzene (0.213 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **9** in 70% (0.225 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.65 (d, J = 4.0 Hz, 1H), 7.63 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 4.0 Hz, 1H), 3.41 (sept, J = 7.5 Hz, 1H), 1.35 (d, J = 7.5 Hz, 6H), 1.34 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 153.6, 152.7, 135.9, 134.8, 129.6, 125.9, 125.7, 123.2, 56.7, 34.2, 30.2, 14.9. Anal. Calcd for $C_{17}H_{22}O_2S_2$ (322.49): C, 63.31; H, 6.88. Found: C, 63.42; H, 6.82.

1-[3-[5-(Propane-2-sulfonyl)-thiophene-2-yl]phenyl]ethanone (10). 3-Bromoacetophenone (0.199 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **10** in 72% (0.222 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.23 (s, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.82 (d, J = 4.0 Hz, 1H), 7.79 (d, J = 4.0 Hz, 1H), 7.63 (t, J = 8.0 Hz, 1H), 3.54 (sept, J = 7.5 Hz, 1H), 2.66 (s, 3H), 1.27 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 198.0, 151.3, 138.2, 136.7, 136.5, 132.8, 131.0, 130.3, 129.3, 126.1, 126.0, 56.3, 27.4, 16.0. Anal. Calcd for $C_{15}H_{16}O_3S_2$ (308.42): C, 58.41; H, 5.23. Found: C, 58.43; H, 5.30.

2-[5-(Propane-2-sulfonyl)thiophene-2-yl]-benzonitrile (11). 2-Bromobenzonitrile (0.182 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **11** in 78% (0.227 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.01 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 4.0 Hz, 1H), 7.85−7.80 (m, 2H), 7.74 (d, J = 4.0 Hz, 1H), 7.70−7.65 (m, 1H), 3.56 (sept, J = 7.5 Hz, 1H), 1.27 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.5, 138.7, 136.1, 135.2, 135.1, 134.5, 130.7, 130.4, 129.4, 118.5, 110.1, 56.4, 16.0. Anal. Calcd for $C_{14}H_{13}NO_2S_2$ (291.39): C, 57.71; H, 4.50. Found: C, 57.88; H, 4.31.

2-Naphthalen-1-yl-5-(propane-2-sulfonyl)thiophene (12). 1-Bromonaphthalene (0.207 g, 1 mmol) and 2-(propane-2-sulfonyl)-thiophene (0.285 g, 1.5 mmol) afford **12** in 77% (0.243 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.15−8.00 (m, 3H), 7.86 (d, J = 4.0 Hz, 1H), 7.70−7.55 (m, 4H), 7.51 (d, J = 4.0 Hz, 1H), 3.59 (sept, J = 7.5 Hz, 1H), 1.32 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 150.1, 137.2, 135.9, 133.9, 130.9, 130.3, 130.0, 129.4, 129.1, 129.0, 127.9, 127.0, 126.0, 124.9, 56.4, 16.1. Anal. Calcd for $C_{17}H_{16}O_2S_2$ (316.44): C, 64.52; H, 5.10. Found: C, 64.41; H, 5.18.

5-[5-(Propane-2-sulfonyl)thiophene-2-yl]pyrimidine (13). 5-Bromopyrimidine (0.159 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **13** in 91% (0.244 g) yield. ^{1}H NMR (300 MHz, MeOD-d_4): δ 9.22 (s, 2H), 9.20 (s, 1H), 7.90 (d, J = 4.0 Hz, 1H), 7.83 (d, J = 4.0 Hz, 1H), 3.55 (sept, J = 7.5 Hz, 1H), 1.28 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, MeOD-d_4): δ 157.8, 153.9, 144.7, 138.7, 135.9, 127.5, 126.5, 56.7, 14.8. Anal. Calcd for $C_{11}H_{12}N_2O_2S_2$ (268.36): C, 49.23; H, 4.51. Found: C, 49.42; H, 4.21.

4-[5-(Propane-2-sulfonyl)thiophene-2-yl]isoquinoline (14). 4-Bromoisoquinoline (0.208 g, 1 mmol) and 2-(propane-2-sulfonyl)-thiophene (0.285 g, 1.5 mmol) afford **14** in 72% (0.228 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.24 (s, 1H), 8.48 (s, 1H), 8.13 (d, J = 8.1 Hz, 1H), 8.07 (d, J = 8.1 Hz, 1H), 7.85−7.65 (m, 2H), 7.72 (t, J = 7.7 Hz, 1H), 7.44 (d, J = 4.0 Hz, 1H), 3.59 (sept, J = 7.5 Hz, 1H), 1.32 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 153.3, 146.3, 142.3, 138.2, 135.4, 133.5, 132.1, 129.2, 128.4, 128.3, 128.1, 124.7, 123.3, 56.7, 14.9. Anal. Calcd for $C_{16}H_{15}NO_2S_2$ (317.43): C, 60.54; H, 4.76. Found: C, 60.41; H, 4.89.

dx.doi.org/10.1021/jo200918n |*J. Org. Chem.* 2011, 76, 6407–6413

4-[5-(Propane-2-sulfonyl)thiophene-2-yl]pyridine (15). 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) and 2-(propane-2-sulfonyl)thiophene (0.285 g, 1.5 mmol) afford **15** in 68% (0.182 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.66 (d, J = 6.0 Hz, 2H), 7.96 (d, J = 4.0 Hz, 1H), 7.84 (d, J = 4.0 Hz, 1H), 7.77 (d, J = 6.0 Hz, 2H), 3.54 (sept, J = 7.5 Hz, 1H), 1.26 (d, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 151.1, 149.0, 139.3, 138.3, 136.7, 127.8, 120.5, 56.3, 15.9. Anal. Calcd for $C_{12}H_{13}NO_2S_2$ (267.37): C, 53.91; H, 4.90. Found: C, 53.81; H, 4.88.

4-(5-Benzenesulfonylthiophene-2-yl)benzaldehyde (16). 4-Bromobenzaldehyde (0.185 g, 1 mmol) and 2-benzenesulfonylthiophene (0.336 g, 1.5 mmol) afford **16** in 72% (0.236 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.04 (s, 1H), 8.03 (d, J = 8.5 Hz, 2H), 8.00 (s, 4H), 7.93 (d, J = 4.0 Hz, 1H), 7.80 (d, J = 4.0 Hz, 1H), 7.74 (t, J = 7.7 Hz, 1H), 7.67 (t, J = 7.7 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 192.9, 150.8, 142.4, 141.7, 137.5, 136.7, 135.8, 134.5, 130.8, 130.4, 127.5, 127.3, 127.1. Anal. Calcd for $C_{17}H_{12}O_3S_2$ (328.41): C, 62.17; H, 3.68. Found: C, 62.24; H, 3.50.

4-(5-Benzenesulfonylthiophene-2-yl)benzonitrile (17). 4-Bromobenzonitrile (0.182 g, 1 mmol) and 2-benzenesulfonylthiophene (0.336 g, 1.5 mmol) afford **17** in 71% (0.231 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.03 (d, J = 8.5 Hz, 2H), 7.95−7.88 (m, 5H), 7.81 (d, J = 4.0 Hz, 1H), 7.74 (t, J = 8.2 Hz, 1H), 7.67 (t, J = 8.2 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 150.1, 142.6, 141.7, 136.5, 135.8, 134.6, 133.7, 130.4, 127.7, 127.5, 127.3, 118.8, 112.1. Anal. Calcd for $C_{17}H_{11}NO_2S_2$ (325.41): C, 62.75; H, 3.41. Found: C, 62.84; H, 3.54.

Methyl 4-(5-Benzenesulfonylthiophene-2-yl)benzoate (18). Methyl 4-bromobenzoate (0.215 g, 1 mmol) and 2-benzenesulfonylthiophene (0.336 g, 1.5 mmol) afford **18** in 73% (0.261 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.03 (d, J = 8.5 Hz, 2H), 8.00 (d, J = 8.5 Hz, 2H), 7.93 (d, J = 4.0 Hz, 1H), 7.87 (d, J = 8.5 Hz, 2H), 7.78−7.60 (m, 4H), 3.86 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 166.0, 150.9, 142.0, 141.7, 136.5, 135.8, 134.5, 130.5, 130.4, 130.3, 127.4, 127.0, 126.8, 52.8. Anal. Calcd for $C_{18}H_{14}O_4S_2$ (358.43): C, 60.32; H, 3.94. Found: C, 60.40; H, 3.79.

2-(5-Benzenesulfonylthiophene-2-yl)benzonitrile (19). 2-Bromobenzonitrile (0.182 g, 1 mmol) and 2-benzenesulfonylthiophene (0.336 g, 1.5 mmol) afford **19** in 76% (0.247 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.10−7.95 (m, 4H), 7.80−7.60 (m, 7H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.6, 143.5, 141.6, 135.2, 135.1, 135.0, 134.6, 134.4, 130.7, 130.5, 130.4, 129.7, 127.5, 118.4, 110.2. Anal. Calcd for $C_{17}H_{11}NO_2S_2$ (325.41): C, 62.75; H, 3.41. Found: C, 62.87; H, 3.37.

5-(4-Cyanophenyl)thiophene-2-sulfonic Acid Diethylamide (20). 4-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **20** in 79% (0.253 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.96 (d, J = 8.5 Hz, 2H), 7.93 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 4.0 Hz, 1H), 7.70 (d, J = 4.0 Hz, 1H), 3.22 (q, J = 7.5 Hz, 4H), 1.11 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.1, 140.7, 136.8, 133.7, 133.3, 127.0, 118.9, 111.6, 42.9, 14.6. Anal. Calcd for $C_{15}H_{16}N_2O_2S_2$ (320.43): C, 56.22; H, 5.03. Found: C, 56.31; H, 5.10.

5-(4-Formylphenyl)thiophene-2-sulfonic Acid Diethylamide (21). 4-Bromobenzaldehyde (0.185 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **21** in 87% (0.281 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.03 (s, 1H), 8.00−7.95 (m, 4H), 7.79 (d, J = 4.0 Hz, 1H), 7.70 (d, J = 4.0 Hz, 1H), 3.21 (q, J = 7.5 Hz, 4H), 1.11 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 192.8, 147.8, 140.5, 137.9, 136.4, 133.3, 130.9, 126.9, 126.7, 43.0, 14.6. Anal. Calcd for $C_{15}H_{17}NO_3S_2$ (323.43): C, 55.70; H, 5.30. Found: C, 55.83; H, 5.21.

Methyl 4-(5-Diethylsulfamoylthiophene-2-yl)benzoate (22). Methyl 4-bromobenzoate (0.215 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **22** in 80% (0.283 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.01 (d, J = 8.5 Hz, 2H), 7.90 (d, J = 8.5 Hz, 2H), 7.77 (d, J = 4.0 Hz, 1H), 7.70 (d, J = 4.0 Hz, 1H), 3.87 (s, 3H), 3.22 (q, J = 7.5 Hz, 4H), 1.11 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 166.1, 147.9, 140.1, 136.8, 133.3, 130.6, 130.1, 126.6, 126.4, 52.8, 42.9, 14.6. Anal. Calcd for $C_{16}H_{19}NO_4S_2$ (353.46): C, 54.37; H, 5.42. Found: C, 54.21; H, 5.30.

5-(4-Acetylphenyl)thiophene-2-sulfonic Acid Diethylamide (23). 4-Bromoacetophenone (0.199 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **23** in 75% (0.253 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.02 (d, J = 8.5 Hz, 2H), 7.89 (d, J = 8.5 Hz, 2H), 7.76 (d, J = 4.0 Hz, 1H), 7.69 (d, J = 4.0 Hz, 1H), 3.21 (q, J = 7.5 Hz, 4H), 2.60 (s, 3H), 1.11 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 197.6, 148.0, 140.1, 137.1, 136.7, 133.3, 129.7, 126.4, 126.3, 43.0, 27.2, 14.6. Anal. Calcd for $C_{16}H_{19}NO_3S_2$ (337.46): C, 56.95; H, 5.68. Found: C, 56.81; H, 5.55.

5-(4-Benzoylphenyl)thiophene-2-sulfonic Acid Diethylamide (24). 4-Bromobenzophenone (0.261 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **24** in 81% (0.323 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.91 (d, J = 8.2 Hz, 2H), 7.80 (d, J = 8.2 Hz, 2H), 7.78−7.65 (m, 5H), 7.56 (t, J = 7.5 Hz, 2H), 3.21 (q, J = 7.5 Hz, 4H), 1.11 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 195.3, 148.0, 140.2, 137.4, 137.3, 136.3, 133.3, 133.2, 131.1, 130.0, 129.1, 126.3, 126.2, 42.9, 14.6. Anal. Calcd for $C_{21}H_{21}NO_3S_2$ (399.53): C, 63.13; H, 5.30. Found: C, 63.23; H, 5.28.

5-(2-Cyanophenyl)thiophene-2-sulfonic Acid Diethylamide (25). 2-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **25** in 79% (0.253 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.99 (d, J = 8.5 Hz, 1H), 7.85−7.77 (m, 2H), 7.75 (d, J = 4.0 Hz, 1H), 7.66 (d, J = 4.0 Hz, 1H), 7.65−7.61 (m, 1H), 3.24 (q, J = 7.5 Hz, 4H), 1.12 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 144.6, 141.3, 135.3, 135.1, 134.4, 132.6, 130.5, 130.1, 128.9, 118.5, 110.0, 42.9, 14.6. Anal. Calcd for $C_{15}H_{16}N_2O_2S_2$ (320.43): C, 56.22; H, 5.03. Found: C, 56.29; H, 5.22.

5-Pyridin-4-ylthiophene-2-sulfonic Acid Diethylamide (26). 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **26** in 91% (0.270 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.63 (d, J = 6.1 Hz, 2H), 7.88 (d, J = 4.0 Hz, 1H), 7.75−7.70 (m, 3H), 3.22 (q, J = 7.5 Hz, 4H), 1.10 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 151.1, 146.2, 141.0, 139.5, 133.2, 127.4, 120.4, 43.0, 14.6. Anal. Calcd for $C_{13}H_{16}N_2O_2S_2$ (296.41): C, 52.68; H, 5.44. Found: C, 52.81; H, 5.34.

5-Isoquinolin-4-ylthiophene-2-sulfonic Acid Diethylamide (27). 4-Bromoisoquinoline (0.208 g, 1 mmol) and thiophene-2-sulfonic acid diethylamide (0.329 g, 1.5 mmol) afford **27** in 86% (0.298 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.39 (s, 1H), 8.61 (s, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.79 (d, J = 4.0 Hz, 1H), 7.78 (t, J = 7.8 Hz, 1H), 7.53 (d, J = 4.0 Hz, 1H), 3.26 (q, J = 7.5 Hz, 4H), 1.14 (t, J = 7.5 Hz, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 154.1, 143.8, 143.4, 140.8, 133.2, 132.7, 132.5, 129.7, 128.9, 128.6, 128.3, 124.2, 123.8, 43.0, 14.7. Anal. Calcd for $C_{17}H_{18}N_2O_2S_2$ (346.47): C, 58.93; H, 5.24. Found: C, 59.04; H, 5.39.

5-(4-Cyanophenyl)thiophene-2-sulfonic Acid Butylphenylamide (28). 4-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid *n*-butylphenylamide (0.443 g, 1.5 mmol) afford **28** in 75% (0.297 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.93 (d, J = 8.5 Hz, 2H), 7.89 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 4.0 Hz, 1H), 7.51 (d, J = 4.0 Hz, 1H), 7.40−7.30 (m, 3H), 7.16 (d, J = 7.8 Hz, 2H), 3.65−3.60 (m, 2H), 1.37−1.22 (m, 4H), 0.80 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 148.0, 138.7, 138.6, 136.7, 134.3, 133.7, 129.6, 128.9, 128.7, 127.0, 126.9, 118.9, 111.7, 50.2, 30.1, 19.4, 13.8. Anal. Calcd for $C_{21}H_{20}N_2O_2S_2$ (396.53): C, 63.61; H, 5.08. Found: C, 63.47; H, 5.01.

5-Naphthalen-1-ylthiophene-2-sulfonic Acid Butylphenylamide (29). 1-Bromonaphthalene (0.207 g, 1 mmol) and thiophene-2-sulfonic acid *n*-butylphenylamide (0.443 g, 1.5 mmol) afford **29** in 82% (0.345 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.03 (d, J = 8.5 Hz,

1H), 8.00 (d, J = 8.3 Hz, 2H), 7.62−7.50 (m, 5H), 7.43−7.30 (m, 4H), 7.21 (d, J = 7.8 Hz, 2H), 3.65 (t, J = 7.5 Hz, 2H), 1.37−1.22 (m, 4H), 0.78 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 148.2, 138.9, 137.8, 133.9, 133.4, 131.0, 130.1, 129.5, 129.1, 129.0, 128.9, 128.7, 128.6, 127.8, 127.0, 125.9, 125.0, 50.1, 30.2, 19.4, 13.8. Anal. Calcd for $C_{24}H_{23}NO_2S_2$ (421.58): C, 68.38; H, 5.50. Found: C, 68.24; H, 5.31.

5-Pyridin-3-ylthiophene-2-sulfonic Acid Butylphenylamide (30). 3-Bromopyridine (0.158 g, 1 mmol) and thiophene-2-sulfonic acid *n*-butylphenylamide (0.443 g, 1.5 mmol) afford **30** in 76% (0.283 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.97 (s, 1H), 8.58 (d, J = 4.7 Hz, 1H), 8.10 (d, J = 7.9 Hz, 1H), 7.73 (d, J = 4.0 Hz, 1H), 7.50 (d, J = 4.0 Hz, 1H), 7.47 (dd, J = 7.9, 4.7 Hz, 1H), 7.40−7.30 (m, 3H), 7.16 (d, J = 7.8 Hz, 2H), 3.65−3.60 (m, 2H), 1.37−1.22 (m, 4H), 0.80 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 150.3, 147.1, 146.7, 138.8, 137.7, 134.2, 133.8, 129.6, 128.9, 128.6, 128.5, 125.9, 124.6, 50.2, 30.1, 19.4, 13.8. Anal. Calcd for $C_{19}H_{20}N_2O_2S_2$ (372.51): C, 61.26; H, 5.41. Found: C, 61.27; H, 5.69.

5-(4-Cyanophenyl)thiophene-2-sulfonic Acid Benzylamide (31). 4-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid benzylamide (0.380 g, 1.5 mmol) afford **31** in 71% (0.251 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.60−8.55 (m, 1H), 7.94−7.91 (m, 4H), 7.74 (d, J = 4.0 Hz, 1H), 7.62 (d, J = 4.0 Hz, 1H), 7.35−7.20 (m, 5H), 4.15−4.12 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 146.9, 142.7, 137.8, 137.0, 133.7, 133.1, 128.7, 128.1, 127.7, 127.0, 126.7, 119.0, 111.6, 46.8. Anal. Calcd for $C_{18}H_{14}N_2O_2S_2$ (354.45): C, 60.99; H, 3.98. Found: C, 60.87; H, 4.20.

5-(4-Acetylphenyl)thiophene-2-sulfonic Acid Benzylamide (32). 4-Bromoacetophenone (0.199 g, 1 mmol) and thiophene-2-sulfonic acid benzylamide (0.380 g, 1.5 mmol) afford **32** in 66% (0.245 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.55−8.52 (m, 1H), 8.03 (d, J = 8.0 Hz, 2H), 7.88 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 4.0 Hz, 1H), 7.62 (d, J = 4.0 Hz, 1H), 7.35−7.20 (m, 5H), 4.15−4.12 (m, 2H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 197.6, 147.8, 142.1, 137.8, 137.1, 136.8, 133.1, 129.7, 128.7, 128.1, 127.7, 126.4, 126.0, 46.8, 27.2. Anal. Calcd for $C_{19}H_{17}NO_3S_2$ (371.48): C, 61.43; H, 4.61. Found: C, 61.57; H, 4.74.

5-(2-Cyanophenyl)thiophene-2-sulfonic Acid Benzylamide (33). 2-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid benzylamide (0.380 g, 1.5 mmol) afford **33** in 74% (0.262 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.65−8.60 (m, 1H), 8.00 (d, J = 8.5 Hz, 1H), 7.85−7.73 (m, 2H), 7.66 (d, J = 4.0 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H), 7.58 (d, J = 4.0 Hz, 1H), 7.35−7.20 (m, 5H), 4.18 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 144.4, 143.6, 137.7, 135.5, 135.1, 134.5, 132.4, 130.5, 130.1, 128.7, 128.6, 128.1, 127.7, 118.6, 110.0, 46.8. Anal. Calcd for $C_{18}H_{14}N_2O_2S_2$ (354.45): C, 60.99; H, 3.98. Found: C, 60.97; H, 4.12.

5-Pyridin-4-ylthiophene-2-sulfonic Acid Benzylamide (34). 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) and thiophene-2-sulfonic acid benzylamide (0.380 g, 1.5 mmol) afford **34** in 73% (0.241 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.64 (d, J = 5.0 Hz, 2H), 7.81 (d, J = 4.0 Hz, 1H), 7.70 (d, J = 5.0 Hz, 2H), 7.64 (d, J = 4.0 Hz, 1H), 7.35−7.20 (m, 5H), 4.15−4.13 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 151.1, 146.0, 143.0, 139.7, 137.7, 133.0, 128.7, 128.1, 127.7, 127.1, 120.4, 46.8. Anal. Calcd for $C_{16}H_{14}N_2O_2S_2$ (330.43): C, 58.16; H, 4.27. Found: C, 58.41; H, 4.10.

5-(4-Cyanophenyl)thiophene-2-sulfonic Acid Phenylamide (35). 4-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid phenylamide (0.359 g, 1.5 mmol) afford **35** in 61% (0.207 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.65−10.55 (m, 1H), 7.88 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 4.0 Hz, 1H), 7.57 (d, J = 4.0 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 7.09 (t, J = 7.8 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.6, 140.9, 137.6, 136.7, 133.9, 133.7, 129.7, 127.0, 126.7, 125.1, 121.0, 118.9, 111.7. Anal. Calcd for $C_{17}H_{12}N_2O_2S_2$ (340.42): C, 59.98; H, 3.55. Found: C, 60.08; H, 3.68.

5-(4-Nitrophenyl)thiophene-2-sulfonic Acid Phenylamide (36). 4-Bromonitrobenzene (0.202 g, 1 mmol) and thiophene-2-sulfonic acid phenylamide (0.359 g, 1.5 mmol) afford **36** in 60% (0.216 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 10.65−10.60 (m, 1H), 8.24 (d, J = 8.5 Hz, 2H), 7.94 (d, J = 8.5 Hz, 2H), 7.74 (d, J = 4.0 Hz, 1H), 7.60 (d, J = 4.0 Hz, 1H), 7.29 (t, J = 7.8 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 7.09 (t, J = 7.8 Hz, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 147.7, 147.0, 141.5, 138.5, 137.6, 134.0, 129.8, 127.4, 127.2, 125.2, 124.9, 121.0. Anal. Calcd for $C_{16}H_{12}N_2O_4S_2$ (360.41): C, 53.32; H, 3.36. Found: C, 53.47; H, 3.47.

5-(4-Cyanophenyl)thiophene-2-sulfonic Acid Phenyl Ester (37). 4-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid phenyl ester (0.360 g, 1.5 mmol) afford **37** in 72% (0.245 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.97 (d, J = 8.5 Hz, 2H), 7.91 (d, J = 8.5 Hz, 2H), 7.85 (d, J = 4.0 Hz, 1H), 7.82 (d, J = 4.0 Hz, 1H), 7.50−7.25 (m, 3H), 7.14 (d, J = 8.2 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 151.2, 149.5, 138.0, 136.1, 133.7, 133.5, 130.7, 128.3, 127.4, 127.2, 122.4, 118.8, 112.4. Anal. Calcd for $C_{17}H_{11}NO_3S_2$ (341.41): C, 59.81; H, 3.25. Found: C, 59.70; H, 3.31.

5-(2-Cyanophenyl)thiophene-2-sulfonic Acid Phenyl Ester (38). 2-Bromobenzonitrile (0.182 g, 1 mmol) and thiophene-2-sulfonic acid phenyl ester (0.360 g, 1.5 mmol) afford **38** in 76% (0.259 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.01 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 4.0 Hz, 1H), 7.82 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 4.0 Hz, 1H), 7.66−7.60 (m, 1H), 7.50−7.30 (m, 3H), 7.15 (d, J = 8.2 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 149.5, 148.7, 137.3, 135.0, 134.7, 134.4, 134.3, 130.8, 130.7, 130.6, 129.3, 128.4, 122.4, 118.3, 110.5. Anal. Calcd for $C_{17}H_{11}NO_3S_2$ (341.41): C, 59.81; H, 3.25. Found: C, 59.97; H, 3.10.

5-(3-Acetylphenyl)thiophene-2-sulfonic Acid Phenyl Ester (39). 3-Bromoacetophenone (0.199 g, 1 mmol) and thiophene-2-sulfonic acid phenyl ester (0.360 g, 1.5 mmol) afford **39** in 75% (0.268 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.23 (s, 1H), 8.03−7.97 (m, 2H), 7.80 (s, 2H), 7.63 (t, J = 7.8 Hz, 1H), 7.48−7.30 (m, 3H), 7.15 (d, J = 8.0 Hz, 2H), 2.65 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 198.0, 152.6, 149.5, 138.2, 138.1, 132.3, 132.0, 131.1, 130.7, 130.4, 129.7, 128.3, 126.2, 125.9, 122.5, 27.4. Anal. Calcd for $C_{18}H_{14}O_4S_2$ (358.43): C, 60.32; H, 3.94. Found: C, 60.41; H, 3.87.

5-Isoquinolin-4-yl-thiophene-2-sulfonic Acid Phenyl Ester (40). 4-Bromoisoquinoline (0.208 g, 1 mmol) and thiophene-2-sulfonic acid phenyl ester (0.360 g, 1.5 mmol) afford **40** in 83% (0.305 g) yield. ^{1}H NMR (300 MHz, DMSO-d_6): δ 9.39 (s, 1H), 8.60 (s, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 3.9 Hz, 1H), 7.88 (t, J = 7.2 Hz, 1H), 7.76 (t, J = 7.2 Hz, 1H), 7.57 (d, J = 3.9 Hz, 1H), 7.50−7.35 (m, 3H), 7.20 (d, J = 8.0 Hz, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 154.6, 149.6, 147.7, 143.9, 137.3, 133.6, 133.1, 132.6, 130.6, 130.1, 128.9, 128.6, 128.3, 128.2, 123.7, 123.6, 122.6. Anal. Calcd for $C_{19}H_{13}NO_3S_2$ (367.44): C, 62.11; H, 3.57. Found: C, 62.20; H, 3.41.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra of compounds **1**−**40**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: henri.doucet@univ-rennes1.fr.

■ ACKNOWLEDGMENT

This research was supported by a CEFIPRA fellowship. We thank the CNRS and "Rennes Metropole" for providing financial support.

REFERENCES

(1) (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (b) Satoh, T.; Miura, M. *Chem. Lett.* **2007**, *36*, 200. (c) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (d) Li, B.-J.; Yang, S.-D.; Shi, Z.-J. *Synlett* **2008**, 949. (e) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269. (f) Ackermann, L.; Vincente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (g) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem* **2010**, *2*, 20.

(2) For recent contributions on direct arylations or vinylations of heteroaromatics from our laboratory, see: (a) Gottumukkala, A. L.; Doucet, H. *Eur. J. Inorg. Chem.* **2007**, 3629. (b) Gottumukkala, A. L.; Derridj, F.; Djebbar, S.; Doucet, H. *Tetrahedron Lett.* **2008**, *49*, 2926. (c) Gottumukkala, A. L.; Doucet, H. *Adv. Synth. Catal.* **2008**, *350*, 2183. (d) Roger, J.; Pozgan, F.; Doucet, H. *J. Org. Chem.* **2009**, *74*, 1179. (e) Fall, Y.; Doucet, H.; Santelli, M. *ChemSusChem* **2009**, *2*, 153. (f) Dong, J. J.; Roger, J.; Požgan, F.; Doucet, H. *Green Chem.* **2009**, *11*, 1832. (g) Roger, J.; Doucet, H. *Adv. Synth. Catal.* **2009**, *351*, 1977. (h) Derridj, F.; Roger, J.; Djebbar, S.; Doucet, H. *Org. Lett.* **2010**, *12*, 4320.

(3) Ohta, A.; Akita, Y.; Ohkuwa, T.; Chiba, M.; Fukunaga, R.; Miyafuji, A.; Nakata, T.; Tani, N.; Aoyagi, Y. *Heterocycles* **1990**, *31*, 1951.

(4) For selected recent examples of direct arylations of thiophenes, see: (a) Fournier Dit Chabert, J.; Chatelain, G.; Pellet-Rostaing, S.; Bouchu, D.; Lemaire, M. *Tetrahedron Lett.* **2006**, *47*, 1015. (b) Nakano, M.; Satoh, T.; Miura, M. *J. Org. Chem.* **2006**, *71*, 8309. (c) David, E.; Pellet-Rostaing, S.; Lemaire, M. *Tetrahedron* **2007**, *63*, 8999. (d) Turner, G. L.; Morris, J. A.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 7996. (e) Amaladass, P.; Clement, J. A.; Mohanakrishnan, A. K. *Tetrahedron* **2007**, *63*, 10363. (f) Nakano, M.; Tsurugi, H.; Satoh, T.; Miura, M. *Org. Lett.* **2008**, *10*, 1851.

(5) For selected examples of palladium-catalysed direct arylations using thiophenes bearing formyl, acetyl, nitrile, halo, silyl, or methyl alcohol substituents, see: (a) Pivsa-Art, S.; Satoh, T.; Kawamura, Y.; Miura, M.; Nomura, M. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 467. (b) Lavenot, L.; Gozzi, C.; Ilg, K.; Orlova, I.; Penalva, V.; Lemaire, M. *J. Organomet. Chem.* **1998**, *567*, 49. (c) Okazawa, T.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2002**, *124*, 5286. (d) Masui, K.; Ikegami, H.; Mori, A. *J. Am. Chem. Soc.* **2004**, *126*, 5074. (e) Chiong, H. A.; Daugulis, O. *Org. Lett.* **2007**, *9*, 1449. (f) Kobayashi, K.; Sugie, A.; Takahashi, M.; Masui, K.; Mori, A. *Org. Lett.* **2005**, *7*, 5083. (g) Derridj, F.; Gottumukkala, A. L.; Djebbar, S.; Doucet, H. *Eur. J. Inorg. Chem.* **2008**, 2550. (h) Roger, J.; Požgan, F.; Doucet, H. *Green Chem.* **2009**, *11*, 425. (i) Liégaut, B.; Lapointe, D.; Caron, L.; Vlassova, A.; Fagnou, K. *J. Org. Chem.* **2009**, *74*, 1826. (j) Dong, J. J.; Roger, J.; Doucet, H. *Tetrahedron Lett.* **2009**, *50*, 2778. (k) Roger, J.; Požgan, F.; Doucet, H. *Adv. Synth. Catal.* **2010**, *352*, 696. (l) Liégault, B.; Petrov, I.; Gorlesky, S. I.; Fagnou, K. *J. Org. Chem.* **2010**, *75*, 1047. (m) Roger, J.; Doucet, H. *Eur. J. Org. Chem.* **2010**, 4412. (n) Chen, L.; Roger, J.; Bruneau, C.; Dixneuf, P. H.; Doucet, H. *Chem. Commun.* **2011**, *47*, 1872.

(6) Join, B.; Yamamoto, T.; Itami, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 3644.

(7) (a) Zhang, Y.-M.; Fan, X.; Yang, S.-M.; Scannevin, R. H.; Burke, S. L.; Rhodes, K. J.; Jackson, P. F. *Bioorg. Med. Chem.* **2008**, *18*, 405. (b) Allsop, G. L.; Cole, A. J.; Giles, M. E.; Merifield, E.; Noble, A. J.; Pritchett, M. A.; Purdie, L. A.; Singleton, J. T. *Org. Proc. Res. Devel* **2009**, *13*, 751.

(8) Shiozaki, M.; Imai, H.; Maeda, K.; Miura, T.; Yasue, K.; Suma, Akira; Masahiro, Y.; Yosuke, O.; Julia, H.; Andrew M., F.; Laird, E. R.; Littmann, N. M.; Andrews, S. W.; Josey, J. A.; Mimura, T.; Shinozaki, Y.; Yoshiuchi, H.; Inaba, T. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 6213.

(9) (a) Davies, D. L.; Donald, S. M. A.; Macgregor, S. A. *J. Am. Chem. Soc.* **2005**, *127*, 13754. (b) Lapointe, D.; Fagnou, K. *Chem. Lett.* **2010**, *39*, 1118.

(10) Ackermann, L.; Althammer, A.; Fenner, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 201.