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One-Pot Synthesis of Symmetrical and Unsymmetrical Aryl Sulfides by Pd-Catalyzed Couplings of Aryl Halides and Thioacetates

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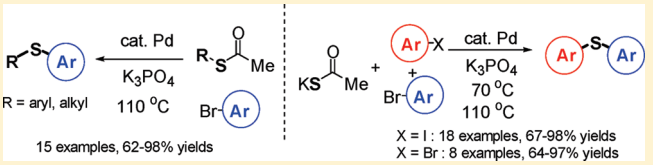
Supporting Information

ABSTRACT: Aryl sulfides were obtained from the coupling reaction of *S*-aryl (or *S*-alkyl) thioacetates and aryl bromides in the presence of palladium catalyst. This reaction method enables the one-pot synthesis of symmetrical and unsymmetrical diaryl sulfides by employing potassium thioacetate with aryl iodides and aryl bromides.



INTRODUCTION

Palladium-catalyzed carbon−carbon and carbon−heteroatom bond formations are practical methods and have been widely employed in organic synthesis.[1] Among carbon−heteroatom bond formations, carbon−nitrogen bond formations have been extensively studied and developed for practical applications since Buchwald and Hartwig independently developed the coupling of aryl halides and amines.[2] The analogous reactions forming carbon−oxygen[3] and carbon−sulfur[4] bonds have also been studied over the past decade. Aryl sulfides are important synthetic intermediates often found in biologically and pharmaceutically active compounds.[5]

Since Migita first reported the coupling reaction of aryl halides with thiols in the presence of $Pd(PPh_3)_4$ as the catalyst and NaO^tBu as a base in polar solvent,[6] palladium-,[4] nickel-,[7] copper-,[8] cobalt-,[9] indium-,[10] and iron-based[11] catalytic systems have been studied for this purpose. In the case of the palladium catalytic system, the development of an efficient ligand has been the main research subject because ligands have played a key role in this transformation.[12] Among them, the Josiphos CyPF-tBu ligand showed high turnover numbers and broad scope in this coupling reaction.[4c−f]

As a source of sulfur in the C−S bond formation, the thiol group has been most often employed in the coupling reaction of aryl halides in the presence of transition-metal catalysts. However, the direct use of thiols has intrinsic drawbacks due to their foul smell, which could lead to a severe environmental problem and, thus, place a ceiling on any large scale process. In addition, they are prone to undergo oxidative homocoupling to produce disulfides as byproducts. To solve these drawbacks, disulfides have been employed,[13] but these require a stoichiometric amount of reductant. Recently, thiourea[14] and potassium thiocyanate[15] have been reported as a sulfur source in the C−S bond formation. However, the former is limited to the aryl alkyl sulfide, and the latter requires high temperature and long reaction time and, moreover, is limited to aryl iodides. Therefore, the development of a foul-smell-free method having a broad scope of aryl halides is needed.

Here, we report a simple, mild, functional group-tolerant system for the synthesis of the symmetrical and unsymmetrical aryl sulfides from potassium thioacetate (**1a**) with aryl halides under thermal conditions. Considering the cost, potassium thioacetate is an excellent sulfur surrogate.[16]

RESULTS AND DISCUSSION

To reach our goal, first, we attempted to find the reaction condition of the direct coupling reaction of thioacetate and aryl halides. The protected thiols such as thiosilate,[4c] thiocyanate,[17] and indium thiolate[18] have been reported in the direct coupling reaction with aryl halides. Lai reported the coupling reaction of potassium thioacetate and aryl bromides to produce *S*-aryl thioacetates under microwave conditions.[19] However, there is no example of the direct coupling reaction of acetyl-protected thiol.[20] As a model reaction, phenyl thioacetate was chosen in the coupling reaction of 4-bromotoluene. The screening for optimized condition was conducted with respect to the ligand, palladium source, base, and solvent. The results were summarized in Table 1.

First, we screened a variety of ligands in the presence of strong base such as NaO^tBu which has been most frequently employed in the C−S bond formation reactions. As expected, monodentate phosphine showed very low yields (entries 1 and 2), and chelating phosphine ligands afforded the desired product in excellent yields (entries 3 and 4). It has been reported that monodentate phosphine showed lower activity than bidentate one in the palladium-catalyzed coupling reaction of thiol and aryl halides.[21] 1,1′-Bis(diphenylphosphino)ferrocene (dppf) was chosen as the ligand after cost consideration.[22] Evaluation of palladium sources revealed that $Pd(dba)_2$ is superior to all other choices. To expand functional group tolerance of this $Pd(dba)_2$/dppf catalytic system, we next examined weak bases in this model coupling reaction. Among the bases screened, K_3PO_4 showed better yields than other weak bases such as Na_2CO_3, K_2CO_3,

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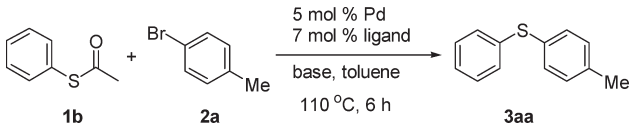
Table 1. Optimization of the Direct C−S Coupling of *S*-Phenyl Thioacetate and 4-Bromotoluene[a]



entry	Pd	ligand	base	conv[b] (%)	yield[b] (%)
1	$Pd(dba)_2$	$BiphP^tBu_2$[c]	NaO^tBu	5	0
2	$Pd(dba)_2$	$BiphPCy_2$[d]	NaO^tBu	2	0
3	$Pd(dba)_2$	Xantphos[e]	NaO^tBu	98	95
4	$Pd(dba)_2$	dppf	NaO^tBu	100	97
5	$Pd(OAc)_2$	dppf	NaO^tBu	100	94
6	$Pd(CH_3CN)_2Cl_2$	dppf	NaO^tBu	72	65
7	$Pd(acac)_2$	dppf	NaO^tBu	60	52
8	$Pd(dba)_2$	dppf	K_3PO_4	72	68
9	$Pd(dba)_2$	dppf	Na_2CO_3	52	45
10	$Pd(dba)_2$	dppf	K_2CO_3	56	34
11	$Pd(dba)_2$	dppf	Cs_2CO_3	48	42
12	$Pd(dba)_2$	dppf	Et_3N	10	7
13[f]	$Pd(dba)_2$	dppf	K_3PO_4	0	0
14[g]	$Pd(dba)_2$	dppf	K_3PO_4	0	0
15[h]	$Pd(dba)_2$	dppf	KOH	0	0
16[i]	$Pd(dba)_2$	dppf	K_3PO_4	100	97

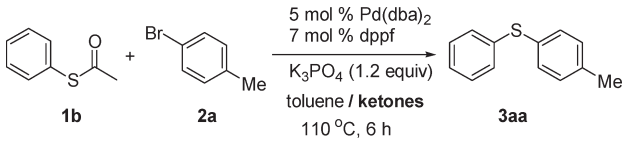
[a] Reaction conditions: *S*-phenyl thioacetate (0.3 mmol), 4-bromotoulene (0.3 mmol), palladium (0.015 mmol), ligand (0.021 mmol), base (0.36 mmol), toluene (0.6 mL) at 110 °C for 6 h in a screw cap vial. [b] Determined by GC analysis with an internal standard of naphthalene. [c] 2-(Di-*tert*-butylphosphino)biphenyl. [d] 2-(Dicyclohexylphosphino)biphenyl. [e] 4,5-Bis-(diphenylphosphino)-9,9-dimethylxanthene. [f] Addition of H_2O (0.3 mL). [g] Addition of MeOH (0.3 mL). [h] Addition of *i*-PrOH (0.3 mL). [i] Addition of acetone (0.3 mL).

Cs_2CO_3, and Et_3N, even though its yield was not higher than NaO^tBu (entries 8−12). When the reactions were carried out in the presence of H_2O or MeOH cosolvents, no desired product was found (entries 13 and 14). And the reaction condition of *i*-PrOH and KOH, which showed good reactivity in the coupling reaction of thiol and aryl idodide,[23] did not produce the coupled product even though it showed 10% conversion yield of 4-bromotoluene (entry 15). Surprisingly, when acetone was added to toluene, the reaction was dramatically improved to give the desired coupling product in quantitative yield (entry 16).[24]

To investigate the role of acetone, a variety of ketones were employed as a cosolvent. The results are summarized in Table 2. When the reaction was carried out with acetone cosolvent in the absence of ligand, no desired product was found (entry 2). This result means that acetone does not work as an activated ligand. When the the amount of acetone was decreased to 0.1 mL, the yield of product decreased (entry 3). However, when the amount of acetone was increased to 1.0 mL, the yield of product did not decrease (entry 4). We obtained similar results in the presence of other ketones such as methyl ethyl ketone, cylcohexanone, and benzophenone instead of acetone (entries 5−7). Although the role of ketone is not clear so far, it can be suggested that it is likely to accelerate the deprotection of *S*-phenyl thioacetate.[25]

Having successfully demonstrated the viability of the $Pd(dba)_2$/dppf-catalyzed direct coupling of aryl bromides with phenyl

Table 2. Role of Ketone in the Direct C−S Coupling of *S*-Phenyl Thioacetate and 4-Bromotoluene[a]



entry	ketone	amount	conv[b] (%)	yield[b] (%)
1	acetone	0.3 mL	100	97
2[c]	acetone	0.3 mL	3	0
3	acetone	0.1 mL	62	56
4	acetone	1.0 mL	100	97
5	methyl ethyl ketone	0.3 mL	100	94
6	cyclohexanone	0.3 mL	95	89
7	benzophenone	3.0 mmol	97	88

[a] Reaction conditions: *S*-phenyl thioacetate (0.3 mmol), 4-bromotoulene (0.3 mmol), $Pd(dba)_2$ (0.015 mmol), 1,1′-bis(diphenylphosphino)ferrocene (0.021 mmol), K_3PO_4 (0.36 mmol), toluene (0.6 mL), at 110 °C for 6 h in a screw cap vial. [b] Determined by GC analysis with an internal standard of naphthalene. [c] In the absence of ligand.

thioacetate, we then proceeded to test the scope and limitations of a variety of thioacetates and aryl bromides. The results are summarized in Table 3. Aryl bromides bearing an electron-donating group such as methyl and methoxy, afforded the corresponding diaryl sulfides in good yields (entries 1−3). Sterically hindered substrates such as 2-bromobiphenyl produced the desired product in 72% yield (entry 4). 4-Bromobenzaldehyde and 2-bromopyridine showed 62% and 82% yields, respectively (entries 5 and 6). *S*-4-Methoxyphenyl thioacetate (**1c**) reacted with 2-bromoanisole to produce the corresponding diaryl sulfide in 67% yield. When *S*-alkyl thioacetates were employed, all thioacetates were coupled with aryl bromides to form alkyl aryl sulfides in high yields. In particular, cynano-substituted thioacetates (**1f**) afforded the coupled products in 81% yield (entry 13), and the benzyl- and *tert*-butyl-substituted thioacetates showed good yields (entries 14 and 15).

We found that 4-iodoanisole reacted with potassium thioacetate (**1a**) to produce only *S*-4-methoxylphenyl thioacetate at 70 °C, even in the presence of bromobenzene, as shown in Scheme 1.[19,26]

This result suggests that this methodology can be applied for the one-pot synthesis of unsymmetrical diaryl sulfide by varying only the reaction temperature. The reactions were carried out in the presence of equal amounts of aryl iodide, aryl bromide, and potassium thioacetate at 70 °C for 3 h and stirred at 110 °C for 6 h. Results are shown in Table 4.

We found that the electronic property of different substituents on the aryl rings did not affect this coupling reaction very much, and aryl halides bearing both electron-withdrawing groups and electron-donating groups worked well. In the case of 1-methoxy-2-(phenylthio)benzene (**5a** and **5k**) and 1-methoxy-3-(phenylthio)benzene (**5b** and **5j**), they could be obtained from both iodobenzene and bromobenzene. Aryl halides bearing ether, amine, ketone, and ester groups afforded the corresponding products in good yields. In addition, heteroaryl sulfides were obtained with satisfactory yields (**5g**−**i**,**o**−**r**).

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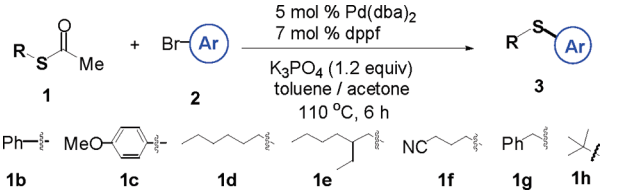
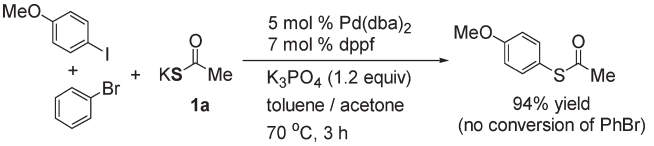
Table 3. C−S Bond Formation of Thioacetates and Aryl Bromides[a]



entry	1	Ar-Br		product		yield (%)
1	**1b**		**2a**		**3ba**	92
2	**1b**		**2b**		**3bb**	91
3	**1b**		**2c**		**3bc**	76
4	**1b**		**2d**		**3bd**	72
5	**1b**		**2e**		**3be**	62
6	**1b**		**2f**		**3bf**	82
7	**1c**		**2h**		**3ch**	67
8	**1d**		**2i**		**3di**	91
9	**1d**		**2a**		**3da**	78
10	**1d**		**2c**		**3dc**	82
11	**1e**		**2i**		**3ei**	87
12	**1e**		**2a**		**3ea**	74
13	**1f**		**2i**		**3fi**	81
14	**1g**		**2i**		**3gi**	98
15	**1h**		**2c**		**3hc**	87

[a] Reaction conditions: thioacetate **1** (3.0 mmol), aryl bromide **2** (3.0 mmol), $Pd(dba)_2$ (0.15 mmol), 1,1′-bis(diphenylphosphino)ferrocene (0.21 mmol), K_3PO_4 (3.6 mmol), toluene (3. 0 mL), acetone (1.5 mL) at 110 °C for 6 h under nitrogen atmosphere; reaction time was not optimized.

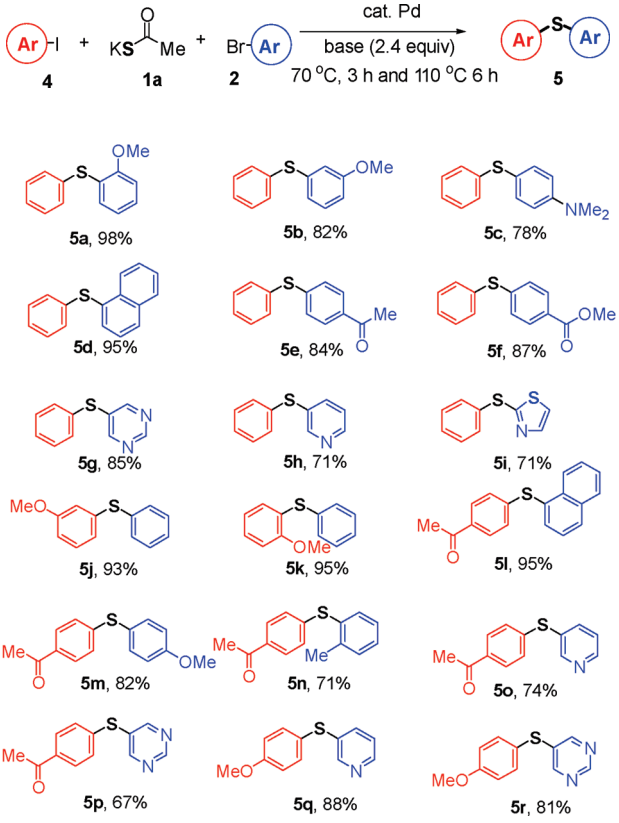
Scheme 1. Competition Reaction of 4-Iodoanisole and Bromobenzene with Potassium Thioacetate[27]



Next, we expanded this reaction condition to the synthesis of the symmetric diaryl sulfide from one-pot reaction of aryl bromides and potassium thioacetate (**1a**). When 2 equiv of aryl bromides and 1 equiv of **1a** were reacted under our optimized conditions, the desired diaryl sulfides were formed. The results are summarized in Table 5.

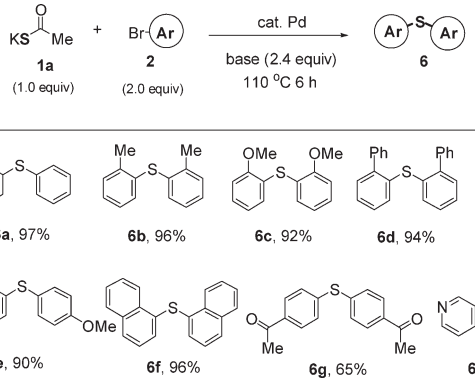
Bromobenzene produced the diphenyl sulfide (**6a**) in 97% yield. Aryl bromides bearing methyl, methoxy, and phenyl at the ortho position, which are sterically demanding substrates, afforded the corresponding diaryl sulfide in good yield (**6b**, **6c**, and **6d**). 4-Bromoanisole and 1-bromonaphthalene showed 90% and 96% yields, respectively (**6e** and **6f**). However, aryl bromides bearing an electron-withdrawing group and heteroaromatic bromide showed slightly lower yields (**6g** and **6h**).

Table 4. Synthesis of Unsymmetrical Diaryl Sulfides[a]



[a] Reaction conditions: potassium thioacetate **1a** (2.0 mmol), aryl bromide **2** (2.0 mmol), aryl iodide **4** (2.0 mmol), $Pd(dba)_2$ (0.2 mmol), 1,1′-bis(diphenylphosphino)ferrocene (0.28 mmol), K_3PO_4 (2.4 mmol), toluene (2.0 mL), acetone (1.0 mL) at 70 °C for 3 h, and subsequently at 110 °C for 6 h under nitrogen atmosphere. Reaction time was not optimized.

Table 5. Synthesis of Symmetrical Diaryl Sulfides.[a]



[a] Reaction conditions: potassium thioacetate **1a** (2.0 mmol), aryl bromide **2** (4.0 mmol), $Pd(dba)_2$ (0.2 mmol), 1,1′-bis(diphenylphosphino)ferrocene (0.28 mmol), K_3PO_4 (2.4 mmol), toluene (2.0 mL), acetone (1.0 mL) at at 110 °C for 6 h. Reaction time was not optimized.

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CONCLUSION

In summary, the directed C−S bond formation from thioacetate has been discovered and successfully applied to the coupling of aryl bromides and a variety of thioacetates. In addition, this reaction condition was applied to the synthesis of symmetric and unsymetric diaryl sulfide by use of potassium thioacetate as a sulfur source. This method provided tolerance to functional groups and foul-smell-free environmental conditions.

EXPERIMENTAL SECTION

Thioacetate **1b** and **1h** were commercially available, and **1c**,[28] **1d**,[29] **1f**,[30] and **1g**[31] were prepared by known procedures.

S-2-Ethylhexyl Ethanethioate (1e). Potassium thioacetate (**1a**) (1.14 g, 10.0 mmol) and 2-ethylhexyl bromide (1.15 g, 6.0 mmol) were placed in a small round-bottomed flask. Toluene (10.0 mL) and acetone (5.0 mL) were then added together. The reaction mixture was stirred for 3 h at 110 °C under nitrogen atmosphere. After completion, the reaction mixture cooled to room temperature. The reaction mixture was poured into 10 mL of saturated aqueous ammonium chloride and extracted with Et_2O (3 × 15 mL). The combined ether extracts were washed with brine (40 mL), dried over $MgSO_4$, and passed through Celite. The product solvent was removed under vacuum, and the resulting crude product was purified by flash chromatography on silica gel. The compound **1e** was obtained with 1.102 g (5.86 mmol, 98%) as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.91 (dd, J = 6.0, 1.8 Hz, 2H), 2.34 (s, 3H), 1.37−1.28 (m, 9H), 0.91−0.86 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 195.8, 39.2, 32.9, 32.4, 30.6, 28.7, 25.6, 22.8, 14.0, 10.8; HRMS (ESI) $[M]^+$ calcd for $C_{10}H_{20}OS$ 188.3362, found 188.3362.

General Procedure for the C−S Bond Formation of Thioacetates and Aryl Bromides. $Pd(dba)_2$ (86.2 mg, 0.15 mmol), 1,1′-bis(diphenylphosphino)ferrocene (116.4 mg, 0.21 mmol), aryl bromides (3.00 mmol), thioacetates (3.00 mmol), and K_3PO_4 (764 mg, 3.60 mmol) were placed in a small round-bottomed flask. Toluene (3.0 mL) and acetone (1.5 mL) were then added together. The reaction mixture was stirred for 6 h at 110 °C under nitrogen atmosphere and then cooled to room temperature. The reaction mixture was poured into 10 mL of saturated aqueous ammonium chloride and extracted with Et_2O (3 × 15 mL). The combined ether extracts were washed with brine (40 mL), dried over $MgSO_4$, and passed through Celite. The solvent was removed under vacuum, and the resulting crude product was purified by flash chromatography on silica gel. The product was eluted with ethyl acetate in hexane.

*4-Tolyl Phenyl Sulfide (**3ba**)*[11c] *(Table 3, Entry 1).* *S*-Phenyl thioacetate (**1b**) (456 mg, 3.00 mmol) was coupled with 4-bromotoluene (**2a**) (513 mg, 3.00 mmol) to give 552 mg (2.76 mmol, 92%) of **3ba** as a pale yellow oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.19 (m, 9H), 2.41 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 137.5, 137.1, 132.2, 131.3, 130.0, 129.8, 129.0, 126.4, 21.1; HRMS (ESI) $[M]^+$ calcd for $C_{13}H_{12}S$ 200.0660, found 200.0662.

*2-Tolyl Phenyl Sulfide (**3bb**)*[4a] *(Table 3, Entry 2).* *S*-Phenyl thioacetate (**1b**) (456 mg, 3.00 mmol) was coupled with 2-bromotoluene (**2b**) (513 mg, 3.00 mmol) to give 546 mg (2.73 mmol, 91%) of **3bb** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31−7.10 (m, 9H), 2.37 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 140.0, 136.1, 133.7, 133.0, 130.6, 129.6, 128.1, 127.9, 126.7, 126.3, 20.6; HRMS (ESI) $[M]^+$ calcd for $C_{13}H_{12}S$ 200.0660, found 200.0662.

*1-Methoxy-4-(phenylthio)benzene (**3bc**)*[8e] *(Table 3, Entry 3).* *S*-Phenyl thioacetate (**1b**) (456 mg, 3.00 mmol) was coupled with 4-bromoanisole (**2c**) (561 mg, 3.00 mmol) to give 494 mg (2.28 mmol, 76%) of **3bc** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (dd, J = 8.7, 2.1 Hz, 2H), 7.25−7.09 (m, 5H), 6.89 (dd, J = 8.7, 2.1 Hz, 2H), 3.81 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 159.8, 138.6, 135.3, 128.9, 128.2, 125.7, 124.3, 115.0, 55.3; HRMS (ESI) $[M]^+$ calcd for $C_{13}H_{12}OS$ 216.0609, found 216.0607.

*2-(Phenylthio)biphenyl (**3bd**)*[32] *(Table 3, Entry 4).* *S*-Phenyl thioacetate (**1b**) (456 mg, 3.00 mmol) was coupled with 2-bromobiphenyl (**2d**) (699 mg, 3.00 mmol) to give 566 mg (2.16 mmol, 72%) of **3bd** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.30 (m, 5), 7.28−7.17(m, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 143.0, 140.6, 135.6, 135.0, 131.8, 131.2, 130.5, 129.3, 129.1, 128.0, 127.9, 127.4, 127.1, 126.7; MS (EI) m/z = 262 (M^+, 100), 229 (14), 184 (28), 152 (14).

*4-(Phenylthio)benzaldehyde (**3be**)*[9] *(Table 3, Entry 5).* *S*-Phenyl thioacetate (**1b**) (456 mg, 1.00 mmol) was coupled with 4-bromobenzaldehyde (**2e**) (555 mg, 3.00 mmol) to give 398 mg (1.86 mmol, 62%) of **3be** as a yellow oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.91 (S, 1H), 7.72 (dd, J = 8.7, 1.8 Hz, 2H), 7.55−7.51 (m, 2H), 7.44−7.41 (m, 3H), 7.24 (dd, J = 8.7, 1.8 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 191.2, 147.3, 134.4, 133.7, 131.3, 130.1, 129.8, 129.2, 127.2; HRMS (ESI) $[M]^+$ calcd for $C_{13}H_{10}OS$ 214.0452, found 214.0459.

*2-(Phenylthio)pyridine (**3bf**)*[33] *(Table 3, Entry 6).* *S*-Phenyl thioacetate (**1b**) (456 mg, 3.00 mmol) was coupled with 2-bromopyridine (**2f**) (474 mg, 3.00 mmol) to give 460 mg (2.46 mmol, 82%) of **3bf** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (dd, J = 4.8, 2.0 Hz, 1H), 7.65−7.58 (m, 2H), 7.48−7.40 (m, 4H), 7.01−6.97 (m, 1H), 6.88 (d, J = 8.0 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 161.5, 149.5, 136.7, 134.9, 131.0, 129.6, 129.0, 121.3, 119.8; HRMS (ESI) $[M]^+$ calcd for $C_{11}H_9NS$ 187.0456, found 187.0456.

*1-Methoxy-2-[(4-methoxyphenyl)thio]benzene (**3ch**)*[33] *(Table 3, Entry 7).* *S*-4-Methoxyphenyl thioacetate (**1c**) (547 mg, 3.00 mmol) was coupled with 2-bromoanisole (**2h**) (561 mg, 3.00 mmol) to give 494 mg (2.01 mmol, 67%) of **3ch** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (dt, J = 8.7, 3.3 Hz, 2H), 7.14−7.06 (m, 1H), 6.89 (dt, J = 8.7, 3.0 Hz, 2H), 6.82 (d, J = 8.1 Hz, 1H), 6.78 (d, J = 4.2 Hz, 2H), 3.87 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 159.8, 155.5, 135.9, 127.9, 127.2, 136.5, 122.6, 121.0, 114.9, 110.2, 55.7, 55.2; HRMS (ESI) $[M]^+$ calcd for $C_{14}H_{14}O_2S$ 246.0715, found 246.0717.

*n-Hexyl Phenyl Sulfide (**3di**)*[34] *(Table 3, Entry 8).* *S*-Hexyl thioacetate (**1d**) (480 mg, 3.00 mmol) was coupled with bromobenzene (**2i**) (471 mg, 3.00 mmol) to give 530 mg (2.73 mmol, 91%) of **3di** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (d, J = 7.2 Hz, 2H), 7.22 (t, J = 7.5 Hz, 2H), 7.10 (t, J = 7.1 Hz, 1H), 2.87 (t, J = 7.4 Hz, 2H), 1.62 (p, J = 7.7 Hz, 2H), 1.39 (p, J = 6.9 Hz, 2H), 1.29−1.23 (m, 4H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 137.5, 129.1, 129.1, 125.9, 33.9, 31.8, 29.5, 28.9, 22.9, 14.4; MS (EI) m/z = 194 (M^+, 75), 123 (30), 110 (100), 77 (9), 65 (9), 43 (9).

*Hexyl p-Tolyl Sulfide (**3da**)*[10b] *(Table 3, Entry 9).* *S*-Hexyl thioacetate (**1d**) (480 mg, 3.00 mmol) was coupled with 4-bromotoluene (**2a**) (513 mg, 3.00 mmol) to give 487 mg (2.34 mmol, 78%) of **3da** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 2.96 (t, J = 7.4 Hz, 2H), 2.4 (s, 3H), 1.72 (p, J = 7.4 Hz, 2H), 1.51 (p, J = 7.5 Hz, 2H), 1.40−1.37 (m, 4H), 0.99 (t, J = 6.9, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 136.0, 133.6, 131.4, 130.0, 129.9, 34.7, 31.7, 29.6, 28.8, 22.9, 21.3, 14.4; MS (EI) m/z = 208 (M^+, 100), 137 (36), 124 (100), 91 (36), 77 (9).

*Hexyl 4-Methoxyphenyl Sulfide (**3dc**)*[35] *(Table 3, Entry 10).* *S*-Hexyl thioacetate (**1d**) (480 mg, 3.00 mmol) was coupled with 4-bromoanisole (**2c**) (561 mg, 3.00 mmol) to give 551 mg (2.46 mmol, 82%) of **3dc** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 9.0 Hz, 2H), 3.78 (s, 3H), 2.80 (t, J = 7.4 Hz, 2H), 1.57 (p, J = 7.5 Hz, 2H), 1.38 (p, J = 7.5 Hz, 2H), 1.28−1.25 (m, 4H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 158.7, 132.9, 127.0, 114.5, 55.3, 35.8, 31.4, 29.3, 28.4, 22.6, 14.1; MS (EI) m/z = 224 (M^+, 100), 153 (18),140 (90), 125 (20), 109 (10).

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*2-Ethylhexyl Phenyl Sulfide (**3ei**) (Table 3, Entry 11).* *S*-2-Ethylhexyl thioacetate (**1e**) (564 mg, 3.00 mmol) was coupled with bromobenzene (**2i**) (471 mg, 3.00 mmol) to give 579 mg (2.61 mmol, 87%) of **3ei** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 7.2 Hz, 2H), 7.12 (t, J = 7.7 Hz, 2H), 7.00 (t, J = 7.2, 1H), 2.78 (d, J = 6.3 Hz, 2H), 1.47 (m, 1H), 1.40−1.22 (m, 4H), 1.18−1.12 (m, 4H), 0.81−0.70 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 137.7, 128.7, 125.4, 38.9, 37.9, 32.4, 28.7, 25.6, 23.0, 14.1, 10.7; MS(EI) m/z = 222 (M^+, 90), 123 (45), 110 (100), 77 (9), 71 (15), 57 (20), 41 (18). Anal. Calcd for $C_{14}H_{22}S$: C, 75.61; H, 9.97; S, 14.42. Found: C, 75.59; H, 9.74; S, 14.08.

*2-Ethylhexyl p-Tolyl Sulfide (**3ea**)[36] (Table 3, Entry 12).* *S*-2-Ethylhexyl thioacetate e (**1e**) (564 mg, 3.00 mmol) was coupled with 4-bromotoluene (**2a**) (513 mg, 3.00 mmol) to give 524 mg (2.22 mmol, 74%) of **3ea** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (d, J = 8.1 Hz, 2H), 7.05 (d, J = 7.8 Hz, 2H), 2.85 (d, J = 6.0 Hz, 2H), 2.28 (s, 3H), 1.54 (m, 1H), 1.47−1.34 (m, 4H), 1.31−1.22 (m, 4H), 0.90−0.83 (m,6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 135.8, 134.3, 129.9, 129.1, 39.3, 39.1, 32.7, 29.1, 25.9, 23.3, 21.3, 14.4, 11.1; MS (EI) m/z = 236 (M^+, 85), 137 (35), 124 (100), 91 (20), 71 (9).

*4-(Phenylthio)butanenitrile (**3fi**)[37] (Table 3, Entry 13).* *S*-3-Cyanopropyl thioacetate (**1f**) (429 mg, 3.00 mmol) was coupled with bromobenzene (**2i**) (471 mg, 3.00 mmol) to give 432 mg (2.43 mmol, 81%) of **3fi** as a pale yellow oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.21 (m, 5H), 3.02 (t, J = 6.8 Hz, 2H), 2.49 (t, J = 7.2 Hz, 2H), 1.94 (p, J = 7.1 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 134.6, 129.9, 129.0, 126.6, 118.9, 32.4, 24.7, 15.8; MS (EI) m/z = 177 (M^+, 100), 123 (80), 110 (40), 77 (10), 65 (10).

*Benzyl Phenyl Sulfide (**3gi**)[34] (Table 3, Entry 14).* *S*-Benzyl thioacetate (**1g**) (498 mg, 3.00 mmol) was coupled with bromobenzene (**2i**) (471 mg, 3.00 mmol) to give 588 mg (2.94 mmol, 98%) of **3gi** as a white solid after chromatography: mp 41−42 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.30 (m, 10H), 4.27 (s, 2H); ^{13}C (75.5 MHz, $CDCl_3$) δ 137.9, 136.9, 130.1, 129.3, 128.9, 127.6, 126.7, 39.4; MS (EI) m/z = 200 (M^+, 70), 109 (9), 91 (100), 65 (15), 51 (5), 39 (5).

*4-Methoxyphenyl 2-Methyl-2-propyl Sulfide (**3hc**)[38] (Table 3, Entry 15).* *S-tert*-Butyl thioacetate (**1h**) (396, 3.00 mmol) was coupled with 4-bromoanisole (**2c**) (561 mg, 3.00 mmol) to give 512 mg (2.61 mmol, 87%) of **3hc** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (m, 2H), 6.84 (m, 2H), 3.79 (s, 3H), 1.25 (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 160.1, 138.8, 123.5, 113.9, 55.1, 45.3, 30.7; MS (EI) m/z = 196 (M^+, 11), 140 (100).

General Procedure for the Synthesis of Unsymmetrical Diaryl Sulfides. $Pd(dba)_2$ (115 mg, 0.20 mmol), 1,1′-bis(diphenylphosphino)ferrocene (155 mg, 0.28 mmol), aryl iodides (2.00 mmol), aryl bromides (2.00 mmol), potassium thioacetates (228 mg, 2.00 mmol), and K_3PO_4 (509 mg, 2.40 mmol) were placed in a small round-bottomed flask. Toluene (2.0 mL) and acetone (1.0 mL) were then added together. The reaction mixture was stirred for 3 h at 70 °C under nitrogen atmosphere. The reaction temperature was increased to 110 °C, and the mixture was stirred for 6 h under nitrogen atmosphere. After completion, the reaction mixture was cooled to room temperature. The reaction mixture was poured into 10 mL of saturated aqueous ammonium chloride and extracted with Et_2O (3 × 15 mL). The combined ether extracts were washed with brine (40 mL), dried over $MgSO_4$, and passed through Celite. The solvent was removed under vacuum, and the resulting crude product was purified by flash chromatography on silica gel. The product was eluted with ethyl acetate in hexane.

*1-Methoxy-2-(phenylthio)benzene (**5a**)[9].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 2-bromoanisole (374 mg, 2.00 mmol) to give 423 mg (1.96 mmol, 98%) of **5a** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.27 (m, 6H), 7.16 (dd, J = 7.5, 1.5 Hz, 1H), 6.97−6.90 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 157.6, 134.9, 132.0, 131.7, 129.4, 128.7, 127.3, 124.4, 121.6, 111.2, 56.2; HRMS (ESI) $[M]^+$ calcd for $C_{13}H_{12}OS$ 216.0609, found 216.0610.

*1-Methoxy-3-(phenylthio)benzene (**5b**)[39].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 3-bromoanisole (374 mg, 2.00 mmol) to give 355 mg (1.64 mmol, 82%) of **5b** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38−7.22 (m, 5H), 7.19 (d, J = 7.8 Hz, 1H), 6.90 (d, J = 6.9 Hz, 1H), 6.86 (m, 1H), 6.77 (ddd, J = 8.4, 2.1, 0.9 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 160.1, 137.2, 135.3, 131.4, 129.9, 129.2, 127.2, 123.0, 115.9, 112.8, 55.3; HRMS (ESI) $[M + Li]^+$ calcd for $C_{13}H_{12}OSLi$ 223.0769, found 223.0767.

*N,N-Dimethyl-4-(phenylthio)benzenamine (**5c**)[9].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 4-bromo-*N,N*-dimethylaniline (400 mg, 2.00 mmol) to give 358 mg (1.56 mmol, 78%) of **5c** as a white solid after chromatography: mp 69−70 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (dd, J = 8.7, 2.1 Hz 2H), 7.22- 7.17 (m, 2H), 7.12−7.05 (m, 3H), 6.71 (d, J = 8.7 Hz, 2H), 2.99 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 150.4, 140.1, 136.0, 128.7, 127.6, 127.0, 125.0, 113.1, 40.4; HRMS (ESI) $[M]^+$ calcd for $C_{14}H_{15}NS$ 229.0925, found 229.0924.

*1-Naphthyl Phenyl Sulfide (**5d**)[8e].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 1-bromonaphthalene (414 mg, 2.00 mmol) to give 449 mg (1.90 mmol, 95%) of **5d** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39−8.36 (m, 1H), 7.84 (t, J = 9.3 Hz, 2H), 7.65 (dd, J = 7.2, 1.2 Hz, 1H), 7.51−7.45 (m, 2H), 7.39 (dd, J = 8.1, 7.2 Hz, 1H), 7.22−6.88 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 136.9, 134.2, 133.5, 132.5, 131.2, 129.2, 129.0, 128.9, 128.5, 126.9, 126.4, 126.1, 125.8, 125.6; HRMS (ESI) $[M + H]^+$ calcd for $C_{16}H_{12}S$ 237.0660, found 237.0661.

*4-Phenylsulfanylacetophenone (**5e**)[11c].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 4-bromoacetophenone (398 mg, 2.00 mmol) to give 384 mg (1.68 mmol, 84%) of **5e** as a yellow solid after chromatography: mp 63−64 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (dt, J = 8.7, 2.1 Hz, 2H), 7.50 (m, 2H), 7.42−7.38 (m, 3H), 7.21 (dt, J = 8.7, 21. Hz, 2H), 2.55 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.1, 144.9, 134.5, 133.8, 132.1, 129.7, 128.9, 128.8, 127.5, 26.4; HRMS (ESI) $[M]^+$ calcd for $C_{14}H_{12}OS$ 228.0609, found 228.0609.

*4-Phenylsulfanylbenzoic Acid Methyl Ester (**5f**)[11c].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and methyl 4-bromobenzoate (430 mg, 2.00 mmol) to give 425 mg (1.74 mmol, 87%) of **5f** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.7 Hz, 2H), 7.50−7.47 (m, 2H), 7.40−7.37 (m, 3H), 7.20 (d, J = 8.7 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 166.7, 144.3, 133.7, 132.4, 130.1, 129.6, 128.6, 127.6, 125.8, 52.1; HRMS (ESI) $[M]^+$ calcd for $C_{14}H_{12}O_2S$ 244.0558, found 244.0556.

*5-(Phenylthio)pyrimidine (**5g**)[40].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 5-bromopyrimidine (318 mg, 2.00 mmol) to give 320 mg (1.70 mmol, 85%) of **5g** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.59 (s, 2H), 7.46−7.37 (m, 5H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 157.0, 156.3, 133.5, 132.7, 131.7, 129.9, 128.8; MS (EI) m/z = 188 (M^+, 100), 160 (13), 134 (20), 77 (8), 5 (8).

*3-(Phenylthio)pyridine (**5h**)[39].* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 3-bromopyridine (316 mg, 2.00 mmol) to give 266 mg (1.42 mmol, 71%) of **5h** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, J = 2.4, 0.6 Hz, 1H), 8.45 (dd, J = 4.2, 1.5 Hz, 1H), 7.58 (dt, J = 8.1, 1.5 Hz, 1H), 7.39−7.27 (m, 5H), 7.20 (ddd, J = 7.2, 4.8, 0.6 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 150.9, 147.7, 137.8, 133.8, 133.5, 131.6, 129.4, 127.8, 123.8; MS (EI) m/z = 187 (M^+, 100), 160 (5), 115 (5), 77 (5), 5 (11), 39 (5).

*2-(Phenylthio)thiazole (**5i**)*[41]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with iodobenzene (408 mg, 2.00 mmol) and 2-bromothiazole (328 mg, 2.00 mmol) to give 275 mg (1.42 mmol, 71%) of **5i** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 3.3 Hz, 1H), 7.63−7.60 (m, 2H), 7.40 (t, J = 4.2 Hz, 3H), 7.21 (d, J = 3.6 Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 165.8, 143.4, 133.6, 131.8, 129.7, 129.4, 120.3; MS (EI) m/z = 193 (M^+, 45), 192(100), 109 (4), 77 (4), 58 (9).

*1-Methoxy-3-(phenylthio)benzene (**5j** = **5b**).* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with bromobenzene (314 mg, 2.00 mmol) and 3-iodoanisole (468 mg, 2.00 mmol) to give 401 mg (1.86 mmol, 93%) of **5j** as a colorless oil after chromatography.

*1-Methoxy-2-(phenylthio)benzene (**5k** = **5a**).* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with bromobenzene (408 mg, 2.00 mmol) and 2-iodoanisole (468 mg, 2.00 mmol) to give 410 mg (1.90 mmol, 95%) of **5k** as a colorless oil after chromatography.

*4-Acetylphenyl Naphthyl Sulfide (**5l**)*[42]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 1-bromonaphthalene (414 mg, 2.00 mmol) and 4-iodoacetophenone (492 mg, 2.00 mmol) to give 529 mg (1.90 mmol, 95%) of **5l** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, J = 8.7 Hz, 1H), 8.04−7.90 (m, 3H), 7.78 (d, J = 8.7 Hz, 2H), 7.59−7.53 (m, 3H), 7.10 (d, J = 8.7 Hz, 2H), 2.54 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.4, 145.7, 135.4, 134.7, 134.5, 134.3, 131.1, 129.1, 129.0, 128.2, 127.8, 127.0, 126.4, 126.2, 126.0, 26.7; MS (EI) m/z = 278 (M^+, 100), 263 (86), 234 (43), 202 (14), 115 (14).

*1-(4-(4-Methoxyphenylthio)phenyl)ethanone (**5m**)*[43]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 4-bromoanisole (374 mg, 2.00 mmol) and 4-iodoacetophenone (492 mg, 2.00 mmol) to give 424 mg (1.64 mmol, 82%) of **5m** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 2.55 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 196.9, 160.5, 146.7, 136.7, 133.7, 128.7, 125.6, 121.2, 115.2, 55.3, 26.3; MS (EI) m/z = 258 (M^+, 100), 243 (83), 215 (12), 200 (12), 184 (10), 171 (12), 139 (12).

*1-[4-(o-Tolylthio)phenyl]ethanone (**5n**)*[44]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 2-bromotoluene (342 mg, 2.00 mmol) and 4-iodoacetophenone (492 mg, 2.00 mmol) to give 344 mg (1.42 mmol, 71%) of **5n** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (dt, J = 8.7, 2.1 Hz, 2H), 7.55 (d, J = 7.2 Hz, 1H), 7.39−7.37 (m, 2H), 7.30−7.26 (m, 1H), 7.12 (dt, J = 8.7, 2.1 Hz, 2H), 2.57 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.0, 144.9, 142.1, 135.8, 133.9, 131.0, 130.2, 129.7, 128.8, 127.1, 126.2, 26.4, 20.6; MS (EI) m/z = 242 (M^+, 81), 227 (100), 184 (37), 165 (7).

*1-[4-(Pyridin-3-ylthio)phenyl]ethanone (**5o**).* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 3-bromopyridine (316 mg, 2.00 mmol) and 4-iodoacetophenone (492 mg, 2.00 mmol) to give 339 mg (1.48 mmol, 74%) of **5o** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51−8.49 (m, 1H), 7.97 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 7.56 (dd, J = 8.1, 1.8 Hz, 1H), 7.18−7.10 (m, 2H), 2.63 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.5, 158.9, 150.3, 139.0, 137.3, 136.7, 133.0, 129.4, 123.8, 121.4, 26.9; HRMS (ESI) $[M]^+$ calcd for $C_{13}H_{11}NOS$ 229.0561, found 229.0562. Anal. Calcd. for $C_{13}H_{11}NOS$: C, 68.09; H, 4.84; N, 6.11; S: 13.98. Found: C, 68.08; H, 4.71; N, 6.14; S, 13.82.

*1-[4-(Pyrimidin-5-ylthio)phenyl]ethanone (**5p**).* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 5-bromopyrimidine (318 mg, 2.00 mmol) and 4-iodoacetophenone (492 mg, 2.00 mmol) to give 309 mg (1.34 mmol, 67%) of **5p** as colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.75 (s, 2H), 7.90 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.7 Hz, 2H), 2.59 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.1, 159.8, 157.9, 140.4, 136.2, 130.7, 129.8, 129.6, 26.8; MS (EI) m/z = 230(M^+, 60), 215 (100), 160 (9), 133 (10), 89 (9). Anal. Calcd for $C_{12}H_{10}N_2OS$: C, 62.59; H, 4.38; N, 12.16; S, 13.92. Found: C, 62.71; H, 4.41; N, 12.15; S, 13.94.

*3-[(4-Methoxyphenyl)thio]pyridine (**5q**)*[33]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 3-bromopyridine (316 mg, 2.00 mmol) and 4-iodoanisole (468 mg, 2.00 mmol) to give 382 mg (1.76 mmol, 88%) of **5q** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (d, J = 3.3 Hz, 1H), 8.35 (dd, J = 4.8, 1.8 Hz, 1H), 7.43−7.40 (m, 3H), 7.10 (ddd, J = 8.1, 4.8, 0.9 Hz, 1H), 6.90 (d, J = 9.0 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 160.5, 149.1, 147.0, 136.3, 135.9, 135.6, 123.9, 122.8, 115.5, 55.6; MS (EI) m/z = 217 (M^+, 100), 202 (39), 173 (22).

*5-(4-Methoxyphenylthio)pyrimidine (**5r**).* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 5-bromopyrimidine (318 mg, 2.00 mmol) and 4-iodoanisole (468 mg, 2.00 mmol) to give 354 mg (1.62 mmol, 81%) of **5r** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.43 (s, 2H), 7.42 (d, J = 9.0 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 161.0, 155.7, 155.3, 136.3, 135.6, 120.6, 115.8, 55.7; MS (EI) m/z = 218 (M^+, 100), 203 (30), 176 (10), 121 (10). Anal. Calcd for $C_{11}H_{10}N_2OS$: C, 60.53; H, 4.62; N, 12.83; S, 14.69. Found: C, 60.80; H, 4.41; N, 12.75; S, 14.94.

General Procedure for the Synthesis of Symmetric Diaryl Sulfides. $Pd(dba)_2$ (115 mg, 0.20 mmol), 1,1′-bis(diphenylphosphino)ferrocene (155 mg, 0.28 mmol), aryl bromides (4.00 mmol), potassium thioacetate (228 mg, 2.00 mmol), and K_3PO_4 (509 mg, 2.40 mmol) were placed in a small round-bottomed flask. Toluene (2.0 mL) and acetone (1.0 mL) were then added in one portion. The reaction mixture was stirred for 6 h at 110 °C under nitrogen atmosphere and then cooled to room temperature. The reaction mixture was poured into 10 mL of saturated aqueous ammonium chloride and extracted with Et_2O (3 × 15 mL). The combined ether extracts were washed with brine (40 mL), dried over $MgSO_4$, and passed through Celite. The solvent was removed under vacuum, and the resulting crude product was purified by flash chromatography on silica gel. The product was eluted with ethyl acetate in hexane.

*Diphenyl Sulfide (**6a**)*[4a]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with bromobenzene (628 mg, 4.00 mmol) to give 361 mg (1.94 mmol, 97%) of **6a** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (m, J = 8 Hz, 4H), 7.30 (m, J = 8 Hz, 4H), 7.25 (m, J = 8 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 135.8, 131.0, 129.2, 127.0; HRMS (ESI) $[M]^+$ calcd for $C_{12}H_{10}S$ 186.0503, found 186.0505.

*2,2′-Ditolyl Sulfide (**6b**)*[45]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 2-bromotoluene (684 mg, 4.00 mmol) to give 412 mg (1.92 mmol, 96%) of **6b** as a white liquid after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.03 (m, 8H), 2.37 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 139.2, 134.6, 131.4, 130.8, 127.4, 127.0, 20.7; MS (EI) m/z = 214 (M^+, 100), 199 (14), 184 (13), 165 (12), 122 (29).

*2,2′-Dimethoxyphenyl Sulfide (**6c**)*[15]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 2-bromoanisole (748 mg, 4.00 mmol) to give 453 mg (1.84 mmol, 92%) of **6c** as a white liquid after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (dt, J = 8.4, 1.8 Hz, 2H), 7.12 (dd, J = 7.5, 1.5 Hz, 2H), 6.94 (t, J = 7.5 Hz, 4H), 3.90 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 158.1. 132.2, 128.7, 122.9, 121.5, 111.1, 56.1; MS (EI) m/z = 246 (M^+, 100), 231 (8), 216 (17), 200 (33), 187 (10), 171 (10).

*2,2′-Biphenyl Sulfide (**6d**).* Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 2-bromobiphenyl (932 mg, 4.00 mmol) to give 636 mg (1.88 mmol, 94%) of **6d** as a white liquid after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43−7.39 (m, 6H), 7.37−7.34 (m, 8H), 7.33−7.30 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 143.9, 141.0, 135.2, 132.7, 130.9, 129.6, 128.3, 128.1, 127.6, 127.3; MS (EI) m/z = 338 (M^+, 100), 184 (26), 152 (14). Anal. Calcd for $C_{24}H_{18}S$: C, 85.17; H, 5.36; S, 9.47. Found: C, 85.22; H, 5.16; S, 9.51.

*4,4′ -Dimethoxyphenyl Sulfide (**6e**)*[33]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 4-bromoanisole (748 mg, 4.00

mmol) to give 443 mg (1.8 mmol, 90%) of **6e** as a yellow liquid after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27 (dt, J = 9.0, 2.4 Hz, 4H), 6.83 (dt, J = 9.0, 2.4 Hz, 4H), 3.78 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 159.0, 132.7, 127.4, 114.7, 55.3; HRMS (ESI) $[M]^+$ calcd for $C_{14}H_{14}O_2S$ 246.0715, found 246.0711.

*1,1′-Dinaphthyl Sulfide (**6f**)*[15]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 1-bromonaphthalene (828 mg, 4.00 mmol) to give 550 mg (1.92 mmol, 96%) of **6f** as a white liquid after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (t, J = 3.3 Hz, 2H), 7.78 (t, J = 6 Hz, 2H), 7.67 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 9.6 Hz, 4H), 7.28−7.17 (m, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 134.5, 133.0, 132.8, 130.3, 129.0, 128.4, 127.2, 126.8, 126.3, 125.5; MS (EI) m/z = 286 (M^+, 100), 271 (7), 252 (27), 142 (9), 126 (9), 115 (11).

*4,4′-Diacetylphenyl Sulfide (**6g**)*[15]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 4-bromoacetophenone (796 mg, 4.00 mmol) to give 351 mg (1.3 mmol, 65%) of **6g** as a colorless oil after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 8.7 Hz, 4H), 7.43 (d, J = 8.4 Hz, 4H), 2.62 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 197.3, 141.3, 136.2, 130.9, 126.5, 26.9; MS (EI) m/z = 270 (M^+, 64), 255 (100), 184 (18), 43 (14).

*3,3′-Dipyridine Sulfide (**6h**)*[15]. Potassium thioacetate (**1a**) (228 mg, 2.00 mmol) was coupled with 3-bromopyridine (632 mg, 4.00 mmol) to give 241 mg (1.28 mmol, 64%) of a colorless oil as after chromatography: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (s, 2H), 8.53 (d, J = 3.9 Hz, 2H), 7.65 (d, J = 7.8 Hz, 2H), 7.26 (t, J = 4.8 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 151.9, 148.9, 138.9, 132.1, 124.4; MS (EI) m/z = 188 (M^+, 100), 161 (14), 78 (13), 51 (14), 39 (12).

■ ASSOCIATED CONTENT

Supporting Information. Spectra of obtained compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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