FULL PAPER

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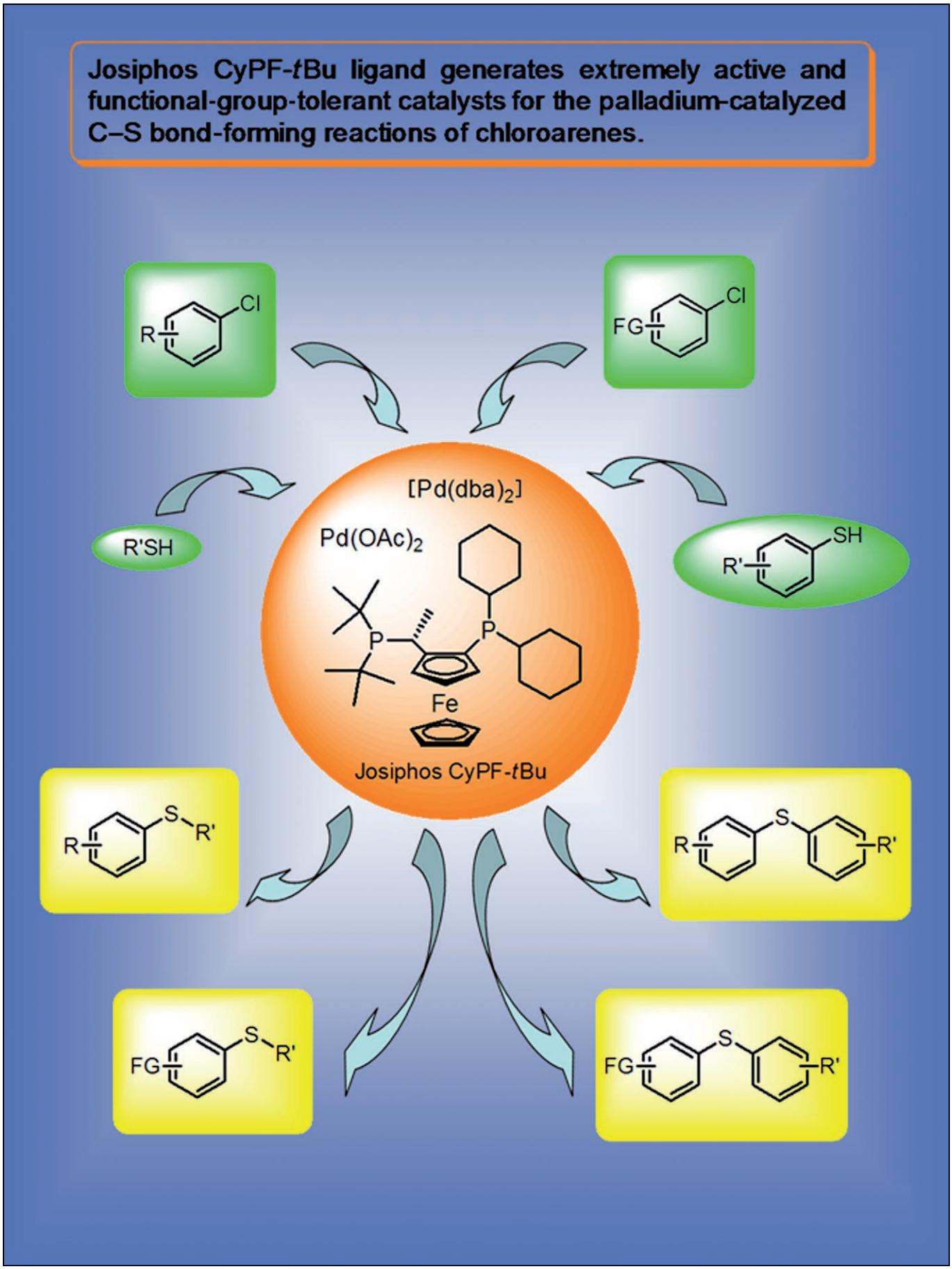
Josiphos CyPF-*t*Bu ligand generates extremely active and functional-group-tolerant catalysts for the palladium-catalyzed C–S bond-forming reactions of chloroarenes.



Pagination corrected Oct. 17, 2006

Highly Efficient and Functional-Group-Tolerant Catalysts for the Palladium-Catalyzed Coupling of Aryl Chlorides with Thiols

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Abstract: The cross-coupling reaction of aryl chlorides with aliphatic and aromatic thiols catalyzed by palladium complexes of the strongly binding bisphosphine CyPF-*t*Bu ligand (**1**) is reported. Most of the reactions catalyzed by complexes of ligand **1** occur with turnover numbers that exceed those of previous catalysts by two orders of magnitude. The reactions occur with excellent yields, broad scope and high tolerance of functional groups. Coupling of aryl halides with thiols in the presence of low loadings of catalysts derived from other Josiphos type ligands, as well as ligands of other structural types, are also described.

Keywords: aryl chlorides · aryl sulfides · cross-coupling · palladium

Introduction

Aryl sulfides[1,2] are valuable intermediates in organic synthesis of biologically and pharmaceutically active molecules, of organic materials, or intermediates to these molecules. A number of aryl sulfides have shown potential clinical applications. These applications include the treatment of inflammation by acting as antagonists of the interaction between leukocyte function-associated antigen-1 and both intracellular adhesion molecule-1 (LFA-1/ICAM-1)[3,4] and vascular cell adhesion molecule-1 (VCAM-1).[5] The applications of aryl sulfides also include treatment of Alzheimer's and Parkinson's diseases by acting as muscarinic[6] or nicotinic[7] receptor antagonists, treatment of asthma and obstructive pulmonary disease by acting as a 5-lipoxygenase inhibitor,[8] treatment of human immunodeficiency virus (HIV) by inhibiting HIV-1 protease[9] and treatment of cancer as tubulin polymerization inhibitors.[10,11] Palladium-catalyzed cross-coupling reactions that form carbon–heteroatom bonds have recently emerged as an extremely powerful synthetic organic method.[12–19] In particular, the synthesis of aromatic amines and ethers from aryl halides or pseudohalides has been extensively studied and developed into practical methodology. In contrast, the analogous synthesis of aryl sulfides has received less attention.[20]

In 1978 and 1980 Migita and co-workers first reported the coupling of iodo- and bromoarenes with thiols in the presence of $[Pd(PPh_3)_4]$ as catalyst.[21,22] In the last decade, more efficient catalyst systems containing bidentate phosphines or dialkylphosphine oxides ligands have been described for this reaction.[23–29] Nevertheless, these protocols display three major drawbacks that reduce their ability to form sulfides in a practical fashion. First, the published catalysts have short lifetimes; low turnover numbers (TON $\leq$ 50) are typically achieved. Second, the coupling of thiols with aryl chlorides is undeveloped, and aryl chlorides are the most useful of the haloarenes because of their wider availability and lower cost.[30] Third, the previous couplings to form sulfides have occurred with narrow scope. The demonstrated tolerance of the reactions to potentially reactive functional groups has been limited to haloarenes containing nitriles and esters.[23–27]

Nickel- and copper-catalyzed coupling of thiols with aryl halides has also been reported.[31,32] However, these processes require either high temperatures or high catalyst loadings. Further, these reactions have typically been conducted with aryl iodides.[33,34]

Palladium thiolates form easily and undergo relatively fast reductive eliminations with aryl groups.[35–37] Thus, the current limitations on the aromatic thiation could result from the notorious sensitivity of late metal catalysts to substrates containing reactive sulfur functionality. The lifetime and concentrations of the catalysts used for the coupling of haloarenes with thiols is likely to be limited by factors such as displacement of dative ligands by thiolates to form anionic thiolate complexes **I** or the formation of bridging thiolate complexes **II** that undergo slow reductive elimination

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(Figure 1).[36] Therefore, a more reactive catalyst for the coupling of thiolates might contain a bisphosphine that binds the metal strongly enough to prevent formation of anionic or bridging thiolate complexes **I** and **II**, while simultaneously promoting oxidative addition and reductive elimination.

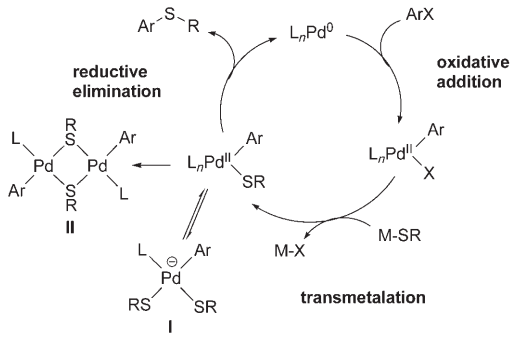
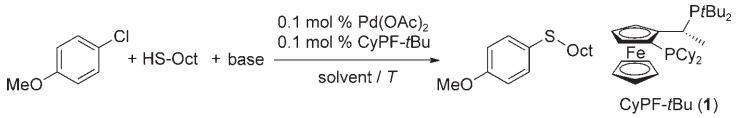


Figure 1. General mechanism for the palladium-catalyzed C–S bond-forming reactions.

Based on this hypothesis, we considered that the restricted backbone conformation, steric hindrance, and strong electron donation of the Josiphos ligand CyPF-*t*Bu (1-dicyclohexylphosphino-2-di-*tert*-butylphosphinoethylferroceno, **1**, in Table 1)[38] could create practical catalysts for the coupling of thiols with aryl halides. In work previously communicated, we have shown that complexes generated from this ligand couple a broad range of thiols with aryl halides and pseudohalides and that reactions conducted with the Josiphos ligand occur with turnover numbers and tolerance of functional groups that far surpass those of previous catalysts.[39] Herein, we report a thorough study of the scope and limitations in the coupling of aryl chlorides with thiols using this catalyst system. In addition, we report an evaluation of other common ligands, as well as a preformed catalyst precursor [(CyPF-*t*Bu)PdCl$_2$], under conditions of low catalyst loading.

Table 1. Optimization of palladium-catalyzed coupling reaction of 4-chloroanisole with 1-octanethiol using CyPF-*t*Bu ligand (**1**).[a]



Entry	Base	Solvent	T [°C][b]	t [h]	Conversion [%] (yield)[c]
1	NaO*t*Bu	DME	100	18	84
2	KO*t*Bu	DME	100	18	80
3	NaHMDS	DME	100	18	57
4	NaO*t*Bu	DME	110	<4	100 (98)
5	KO*t*Bu	DME	110	18	94 (87)
6	NaO*t*Bu	1,4-dioxane	110	5	100 (94)
7[d]	NaO*t*Bu	DME	110	48	93 (85)
8[e]	NaO*t*Bu	DME	110	7	100 (96)

[a] All the experiments were conducted with a 1:1 ratio of metal to ligand, 1 mmol of both 4-chloroanisole and 1-octanethiol, and 1.1 equiv base in 1.5 mL solvent. [b] Bath temperature. [c] Determined by GC analysis. Isolated yields are indicated in parentheses. [d] 0.05% catalyst loading employed. [e] [Pd(dba)$_2$] used as palladium precursor.

Results and Discussion

Establishment of reaction conditions: We initially selected the coupling of electron-rich 4-chloroanisole with 1-octanethiol as model system to assess the catalyst activity and to determine the optimum reaction conditions. The experiments were conducted using equimolecular amounts of 0.1 mol% Pd(OAc)$_2$ and CyPF-*t*Bu ligand **1** and several bases (1.1 equiv), solvents and reaction temperatures (Table 1). Reactions containing different bases were conducted at 100°C in DME (1,2-dimethoxyethane),[40] and the formation of aryl sulfide was measured by GC after 18 h. Reactions conducted with NaO*t*Bu, KO*t*Bu and NaHMDS (NaN(SiMe$_3$)$_2$) occurred with moderate to good conversions (Table 1, entries 1–3), while reactions with weaker carbonate, phosphate and amine bases (not listed in Table 1) occurred to <5% conversion and formed large amounts of dioctyldisulfide.

Reactions at 110°C occurred to higher conversions. Reactions at this temperature conducted with NaO*t*Bu as base occurred to full conversion in less than 4 h and with an excellent yield of sulfide (Table 1, entry 4). In contrast, reactions conducted with KO*t*Bu base proceeded to 94% conversion and 87% isolated yield after 18 h (Table 1, entry 5). Reactions conducted with NaO*t*Bu in 1,4-dioxane occurred in high yield after similar times as the reactions with NaO*t*Bu in DME (Table 1, entry 6), while reactions in other solvents, such as toluene, DMF or DMSO, formed only traces of the desired aryl sulfide.

Further studies were also conducted to fine-tune the catalyst loading and palladium precursor. These studies revealed that a decrease in the catalyst loading to 0.05% resulted in incomplete conversion of this electron-rich chloroarene, even at extended reaction times (Table 1, entry 7). However, reactions of electron-neutral and electron-poor chloroarenes described later in this paper do occur with lower loadings. These studies also showed that the catalyst system derived from [Pd(dba)$_2$] and the one derived from Pd(OAc)$_2$ are similar, but that the one derived from [Pd(dba)$_2$] reacts slightly slower (Table 1, entry 8).

Ligand influence on the thiation of aryl chlorides at low catalyst loadings: After having established conditions for the coupling of chloroarenes with alkyl thiols using the combination of Pd(OAc)$_2$ and CyPF-*t*Bu as catalyst, we surveyed palladium complexes of a series of ligands for these reactions at low catalyst loadings. The structures of these ligands and a summary of the results of this study are shown in

Figure 2. Each reaction was conducted at 110 °C for 24 h with 0.1 mol % of ligand and $Pd(OAc)_2$, and conversions to the desired sulfide were measured by GC.

Reactions were conducted with several members of the Josiphos family of ligands (**1**–**6**) as well as bidentate phos-

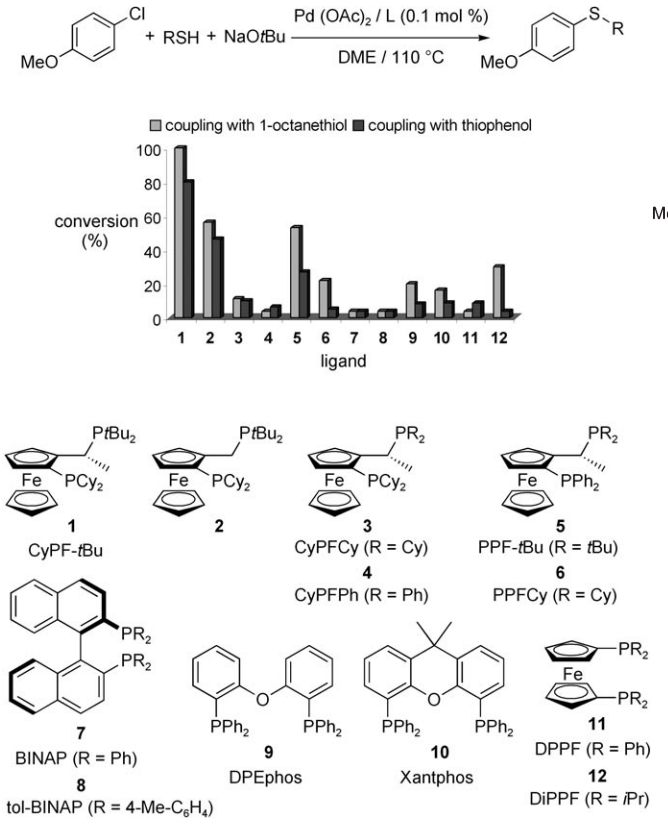
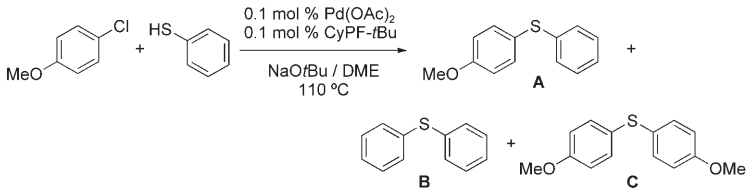


Figure 2. Effect of ligand on the coupling of aryl chlorides with thiols at 0.1 mol % catalyst loading. Reaction conditions: 4-chloroanisole (1 mmol), RSH (1 mmol), $Pd(OAc)_2$/ligand (0.1 mol %), NaO*t*Bu (1.1 mmol) in DME (1.5 mL) at 110 °C for 24 h.

phines **7**–**12** that were previously reported for couplings of aryl halides with thiols. Among the Josiphos family of ligands, CyPF-*t*Bu (**1**) clearly generated the most active catalyst, affording full conversion to the aryl sulfide in less than 4 h. Reactions catalyzed by complexes of Josiphos-type ligands **2** and **5**, which are less rigid and less electron donating than **1**, occurred to moderate conversions (ca. 50 %), even after 24 h. Reactions conducted with the less sterically demanding analogues **3**, **4** and **6** formed moderate to small amounts of the desired sulfide. Catalysts based on BINAP, tol-BINAP or DPPF were completely ineffective for this coupling. Catalysts based on DPEphos, Xantphos and even DiPPF, which were reported to promote thiations of unactivated chloroarenes under similar reaction conditions but with higher catalyst loading,[25] afforded conversions of less than 30 % when used in 0.1 mol % quantities.

A parallel study of the coupling of 4-chloroanisole with thiophenol was conducted. The reactions of thiophenol conducted with the Josiphos ligands **1**–**6** occurred in a similar fashion to the reactions of 1-octanethiol. Also similar to the reactions of the alkane thiol, reactions of thiophenol catalyzed by complexes of the other bisphosphines, including DPEphos, Xantphos and DiPPF, occurred in low yield. Thus, CyPF-*t*Bu (**1**) clearly generated the most active catalyst for the coupling of thiophenol.

Under the standard conditions developed, however, 4-methoxyphenyl phenyl sulfide **A** was formed with significant amounts of undesired symmetrical sulfides **B** and **C** (Scheme 1). Formation of these by-products was first de-



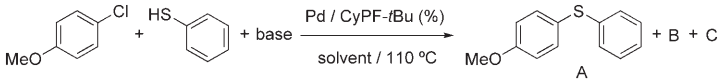
Scheme 1. By-products formed from the coupling of 4-chloroanisole with thiophenol.

scribed for a nickel-catalyzed C–S bond-forming reaction, and a tentative mechanism for the aryl–aryl scrambling was proposed.[41] The amount of symmetrical sulfides formed from reactions of electron-deficient aryl halides and/or electron donating aromatic thiols is lower than the amount of these side products formed from reactions of electron-rich or electron-neutral aryl halides. For example, large amounts of these symmetrical byproducts were observed from the coupling of unactivated chloroarenes with an electron-rich aromatic thiol in the presence of the combination of $Pd(OAc)_2$ and DiPPF as catalyst. The formation of these by-products was suppressed by the use of NEt_3 as solvent.[25]

To prevent the formation of the symmetrical diaryl sulfides we determined the effect of base, solvent, and catalyst loading for the reaction of 4-chloroanisole with thiophenol. These results are summarized in Table 2. A significant dependence of the amount of side product on the nature of the base and its counterion was observed. The quantity of symmetrical sulfides was only 2 % when the reaction was conducted with KO*t*Bu as base, rather than 9 % when it was conducted with NaO*t*Bu (Table 2, entries 1 and 2); significant amounts of **B** and **C** were formed from reactions conducted with NaHMDS and LiHMDS as base (Table 2, entries 3–4). Reactions conducted with other bases such as NaOH, carbonates and amines gave low conversions to products.

The solvent also affected the amount of the side products **B** and **C**. Reactions in 1,4-dioxane and toluene formed lower amounts of **B** and **C**. Even with NaO*t*Bu as base, only 4 % of these materials were formed in these two solvents. Ultimately, the highest isolated yield and selectivity were achieved when the reactions were conducted in toluene in the presence of KO*t*Bu as base (Table 2, entries 5–8). Reactions in toluene with KO*t*Bu as base in the presence of only 0.1 mol % catalyst afforded the coupled product after 6 h at 110 °C in high yields with less than 1 % of the side products (Table 2, entry 9).

Table 2. Optimization of palladium-catalyzed coupling reaction of 4-chloroanisole with thiophenol using CyPF-*t*Bu ligand (**1**).[a]



Entry	Base	Solvent	Pd source	Loading [%]	*t* [h]	A:B:C [%][b]
1	NaO*t*Bu	DME	$Pd(OAc)_2$	0.5	12	91:4:5
2	KO*t*Bu	DME	$Pd(OAc)_2$	0.5	12	98 (93):1:1
3	NaHMDS	DME	$Pd(OAc)_2$	0.5	12	71:15:14
4	LiHMDS	DME	$Pd(OAc)_2$	0.5	12	56:24:20
5	NaO*t*Bu	1,4-dioxane	$Pd(OAc)_2$	0.5	12	96:2:2
6	KO*t*Bu	1,4-dioxane	$Pd(OAc)_2$	0.5	12	97 (87):2:1
7	NaO*t*Bu	toluene	$Pd(OAc)_2$	0.5	12	98 (93):1:1
8	KO*t*Bu	toluene	$Pd(OAc)_2$	0.5	12	>98 (97):1:<1
9	KO*t*Bu	toluene	$Pd(OAc)_2$	0.1	6	>98 (95):<1:<1
10	KO*t*Bu	toluene	$[Pd(dba)_2]$	0.5	12	>99.5 (98):<0.5:–
11	KO*t*Bu	toluene	$[Pd(dba)_2]$	0.1	<4	>99.5 (98):<0.5:–

[a] All the experiments were conducted with a 1:1 ratio of metal to ligand, 1 mmol of both 4-chloroanisole and thiophenol, and 1.1 equiv base at 110 °C in 1.5 mL solvent. [b] Distribution of sulfides determined by GC. Isolated yield of desired sulfide A is indicated in parentheses.

The palladium source also affected the amount of side product. Reactions conducted with $[Pd(dba)_2]$ and Josiphos ligand **1** as catalyst generated only traces (<0.5%) of byproduct (Table 2, entry 10). Reactions conducted with only 0.1 mol% $[Pd(dba)_2]$ and Josiphos ligand **1** occurred in high yield in less than 4 h to form the desired diaryl sulfide in essentially quantitative yield (Table 2, entry 11).

Thus, our studies on reaction conditions showed that the combination of $Pd(OAc)_2$/CyPF-*t*Bu/NaO*t*Bu/DME was most effective for the coupling of aryl chlorides with aliphatic thiols and that the combination of $[Pd(dba)_2]$/CyPF-*t*Bu/KO*t*Bu/toluene was most effective for reactions of aromatic thiols. Reactions under the standard conditions, but without catalyst, formed mostly disulfides. Less than 5% of the aryl sulfide was formed.

Scope of the reaction—Coupling of unactivated aryl chlorides: Reactions of a series of aryl chlorides with aliphatic and aromatic thiols were conducted under the optimized reaction conditions with the combination of palladium and Josiphos ligand **1** as catalyst; the results are given in Tables 3 and 4.

Reactions of aliphatic thiols with chloroarenes are summarized in Table 3. These data show that primary, secondary, and tertiary aliphatic thiols reacted to form the corresponding sulfides in excellent yields within short reaction times. Reactions were conducted with catalyst loadings in the range of 0.01 to 0.1 mol%. These loadings are one or two orders of magnitude lower than those in previous studies of this reaction (Table 3, entries 1–7, 9–10, 12–16). For instance, the coupling of chlorobenzene with 1-octanethiol occurred in 85% yield with only 100 ppm of catalyst, corresponding to a turnover number of 8500 (Table 3, entry 4). This value is more than two orders of magnitude higher than that for the analogous coupling of an unactivated chloroarene with a primary thiol catalyzed by the combination of $Pd(OAc)_2$ and DiPPF (48 turnovers).[25] Further attempts to decrease the catalyst loading of reactions conducted with the Josiphos ligand by increasing the temperature to 140 °C in a sealed reaction vessel or by changing the solvent to diethylene glycol diethyl ether (b.p. 188 °C) led to incomplete conversions and formation of disulfide side product.

Sterically demanding *ortho*-substituted chloroarenes coupled in high yield using catalyst loadings up to 0.5 mol% (Table 3, entries 13 and 18–21). Even a di-*ortho*-substituted chloroarene reacted with a hindered tertiary thiol, although a higher catalyst loading and long reaction time were necessary to achieve good yield and conversion in this case (Table 3, entry 22). Reactions could also be conducted at lower temperatures (70 °C) by simply increasing the amount of catalyst to 2.0 mol% and increasing reaction times to 24 h (Table 3, entries 8, 11 and 17).

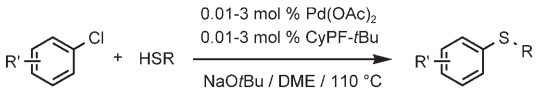
Although a majority of the reactions was assembled in a drybox, identical catalyst activity was observed for reactions performed under inert atmosphere using common Schlenk techniques (Table 3, compare entries 3 and 5). Using these techniques, the coupling reaction was conducted with 5 mmol of chlorobenzene without a decrease in yield or catalyst efficiency (Table 3, entry 6).

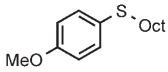
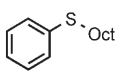
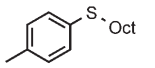
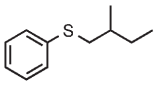
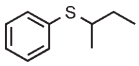
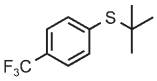
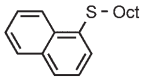
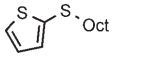
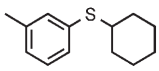
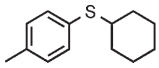
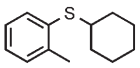
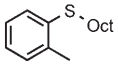
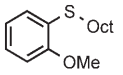
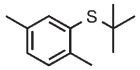
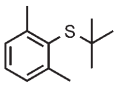
Studies on the scope of the coupling of arene thiols are summarized in Table 4. Again, very high yields in short reaction times were obtained using one or two orders of magnitude less catalyst loading than was needed for analogous couplings with prior systems. In contrast to prior reactions that occurred in high yields with the combination of unactivated chloroarenes and electron-rich arenethiols or electron-deficient chloroarenes with electron-neutral aromatic thiols,[25] the current system coupled either electron-rich, electron-neutral or electron-deficient chloroarenes with electron-rich or electron-neutral aromatic thiols.

Unhindered chloroarenes reacted with aromatic thiols without formation of side products in the presence of 0.05–0.5 mol% catalyst (Table 4, entries 1–3, 5–12). No significant increase in the loading was necessary for the coupling of sterically demanding aromatic thiols, even when electron-rich aryl chlorides were used (Table 4, entries 13–14). Reactions conducted at lower temperature (70 °C) occurred to high conversion and in good yield after 48 h in the presence of 3.0 mol% catalyst (Table 4, entry 4).

Reactions of *ortho*-substituted chloroarenes also occurred, but some of these couplings were accompanied by formation of symmetrical diaryl sulfide side products. The reactions of electron-rich thiols with *ortho*-substituted chloroarenes and the reaction of 2-chloroanisole with thiophenol occurred in

Table 3. Palladium-catalyzed coupling of aryl chlorides with alkyl thiols using CyPF-*t*Bu ligand.[a]

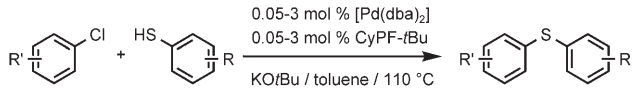


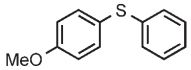
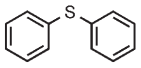
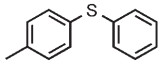
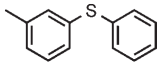
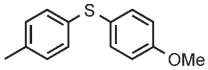
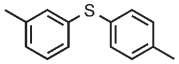
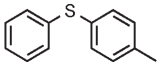
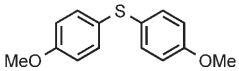
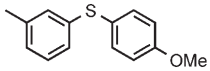
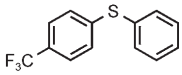
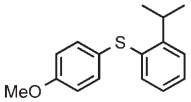
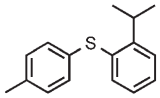
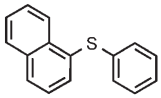
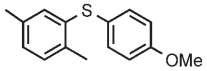
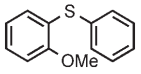
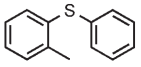
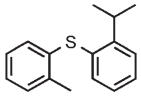
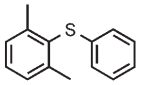
Entry	Cat. [mol %]	Yield [%][b]	Product
1	0.1	98	
2	0.1	91	
3	0.05	91	
4	0.01	85	
5[c]	0.05	92	
6[c,d]	0.05	93	
7	0.05	97	
8[e]	2.0	97	
9	0.05	95	
10	0.05	91	
11[e]	2.0	89	
12	0.1	82	
13	0.05	92	
14	0.05	96	
15	0.05	98	
16	0.05	97	
17[e]	2.0	91	
18	0.25	90	
19	0.25	95	
20	0.25	97	
21	0.5	89	
22	3.0	77[f]	

[a] All experiments were conducted with a 1:1 ratio of metal to ligand, 1 mmol of both chloroarene and alkyl thiol, and NaO*t*Bu (1.1 equiv) in DME (1.5 mL) for 2–24 h at 110 °C. [b] Isolated yield of an average of two runs. [c] Reactions performed without using a drybox. [d] 5 mmol scale. [e] Reaction performed at 70 °C. [f] 82 % conversion after 36 h.

high yields without formation of side products (Table 4, entries 17–18). The reaction of 1-chloronaphthalene with thiophenol in the presence of only 0.1 mol % catalyst formed the coupled product in good yield, but 10 % of the undesired symmetrical sulfides also formed. This side product was eliminated by conducting the reaction at the lower temperature of 90 °C (3 mol % catalyst). The reactions of 2-chlorotoluene with thiophenol and with 2-isopropylbenzenthiol did

Table 4. Palladium-catalyzed coupling of aryl chlorides with aryl thiols using CyPF-*t*Bu ligand.[a]



Entry	Cat. [mol %]	Yield [%][b]	Product
1	0.1	98	
2	0.1	95	
3	0.1	95	
4[c]	3.0	83	
5	0.1	98	
6	0.05	86	
7	0.1	95	
8[d]	0.1	93	
9[d]	0.25	98	
10	0.25	99	
11	0.25	97	
12	0.5	89	
13	0.25	94	
14	0.25	97	
15[e]	0.1	84	
16[f]	3.0	95	
17	1.0	92	
18	1.0	97	
19[g]	0.5	70	
20[g]	0.25	70	
21	3.0	–	

[a] All experiments were conducted with a 1:1 ratio of metal to ligand, 1 mmol of both chloroarene and aryl thiol, and KO*t*Bu (1.1 equiv) in toluene (1.5 mL), requiring 2–24 h of heating at 110 °C to complete. [b] Isolated yield of an average of two runs. [c] Reaction conducted at 70 °C and stopped after 48 h at 90 % conversion. [d] 1.1 equiv LiHMDS were used as base. [e] ~10 % symmetrical sulfides were observed. [f] Reaction conducted at 90 °C. [g] ~20 % symmetrical sulfides were observed.

not occur at the lower temperature, and reactions at 110 °C in the presence of 0.25–0.5 mol % catalyst formed the coupled products in 70 % yield with about 20 % of side products (Table 4, entries 19–20). Further, the reaction of 2,6-dimethyl chlorobenzene with thiophenol did not occur (Table 4, entry 21).

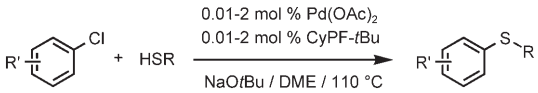
Coupling of functionalized aryl chlorides: The efficiency of the present catalyst system prompted us to evaluate the tolerance of this process to the presence of functional groups that might be expected to poison the catalyst or to react with thiolate nucleophiles. The coupling of a wide range of functionalized aryl chlorides with aliphatic thiols is summarized in Table 5. Chloroarenes bearing a nitrile, ketone, carboxylic acid, amide, protected or free amino groups, and aromatic or aliphatic hydroxyl groups coupled under the standard conditions to form the corresponding aryl sulfide in good to excellent yields (Table 5, entries 1–8 and 12–18). The catalyst loading for some of these reactions are extremely low, and even reactions of electron-rich and hindered substrates occurred with loadings at or below 2.0 mol %.

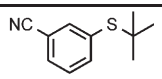
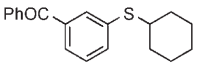
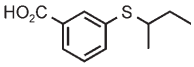
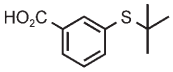
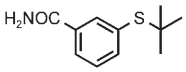
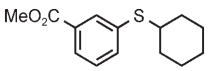
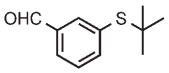
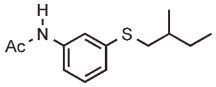
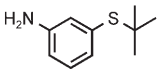
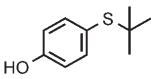
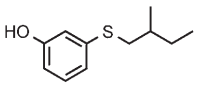
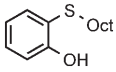
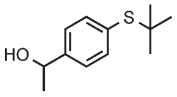
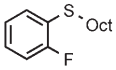
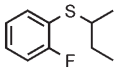
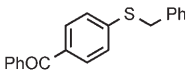
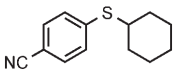
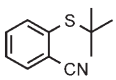
Reactions of aryl chlorides with ester or aldehyde functionalities that occur in modest yield or are incompatible with nucleophilic alkoxide bases occurred in high yield in the presence of the weaker Cs_2CO_3 base (Table 5, entries 10, 11). However, couplings of chloroarenes possessing enolizable keto functionality were unsuccessful, even with weaker bases (not included in Table 5). Although both the rate and the yield of the formation of sulfides from chloroarenes containing electron-withdrawing groups in the *para*- and *ortho*-positions were higher in the presence of our catalyst system than in the absence of catalyst, uncatalyzed processes did occur in good yields and conversions after longer times (24–48 h vs <4 h with the palladium catalyst) at 110 °C (Table 5, entries 21, 23, 25 vs 22, 24, 26) with the electron-poor chloroarenes.

The reaction of 1-chloro-2-fluorobenzene with 1-octanethiol gave a mixture of the expected aryl sulfide product and a small amount (8 %) of *ortho*-chlorophenyl sulfide from reaction at the C–F bond (Table 5, entry 19). Nevertheless, the analogous reaction with a secondary thiol in the presence of 0.25 mol % of catalyst afforded the expected *ortho*-fluorophenyl sulfide with only traces of product from thiation of both carbon–halogen bonds (Table 5, entry 20). We envisioned that the minor side product could be formed by an uncatalyzed nucleophilic substitution at the activated C–F bond. Indeed, reaction of 1-chloro-2-fluorobenzene with 1-octanethiol in the absence of catalyst afforded 75 % conversion to the product from substitution at the fluoride, and the C–Cl bond remained intact, as shown in Scheme 2. In contrast to these results with electron-poor aryl fluorides, no C–S bond formation was detected from reaction of unactivated aryl fluorides, such as 1-fluoro-4-methylbenzene, in the presence of catalyst (Scheme 2).

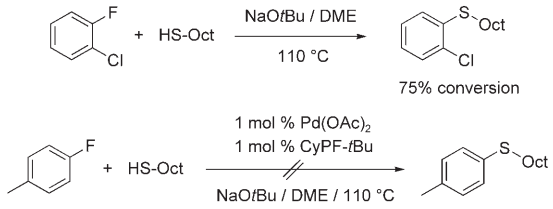
The scope of reactions of functionalized aryl chlorides with aromatic thiols is summarized in Table 6. In contrast to

Table 5. Palladium-catalyzed coupling of functionalized aryl chlorides with aliphatic thiols using CyPF-*t*Bu ligand.[a]



Entry	Cat. [mol %]	Yield [%][b]	Product
1[c]	0.05	90	
2[c]	0.01	79	
3[c]	0.05	86	
4	0.1	76	
5	0.05	67	
6	0.01	71	
7	0.05	98	
8	0.01	91	
9[d]	0.1	56	
10[e]	0.5	72	
11[e]	0.25	91	
12	0.25	99	
13[e]	0.25	96	
14	1.0	91	
15	0.5	85	
16	2.0	97	
17[d]	0.5	93	
18[e]	0.5	67	
19	0.1	78[f]	
20	0.25	98[g]	
21[c]	0.01	93	
22[c,h]	-	86	
23[c]	0.01	90	
24[c,h]	–	79 (91)	
25[c]	0.25	80	
26[c,h]	–	77	

[a] All experiments were conducted with a 1:1 ratio of metal to ligand, 1 mmol of both chloroarene and alkyl thiol, and 2.4 equiv NaO*t*Bu, unless otherwise stated, in DME (1.5 mL), requiring 2–6 h of heating at 110 °C to complete. [b] Isolated yield of an average of two runs. Conversions in incomplete reactions indicated in parentheses. [c] 1.1 equiv NaO*t*Bu were employed. [d] 1.02 equiv NaO*t*Bu were used. [e] Reaction performed using 1.1 equiv $CsCO_3$ as base. [f] Estimated by ^{1}H NMR (400 MHz) of a mixture with the related aryl sulfide from the reaction at C–F bond (8 % yield). [g] Traces of dithiolation product were observed. [h] Uncatalyzed reaction.

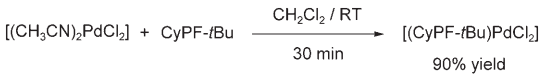


Scheme 2. Nucleophilic aromatic substitution of activated fluoroarenes.

the couplings of less functionalized chloroarenes, no symmetrical sulfides were detected from reaction of the chloroarenes in Table 6 under the standard conditions involving $Pd(OAc)_2$ and ligand **1** as catalyst, NaO*t*Bu as base and DME as solvent. Like the reactions of aliphatic thiols, the coupling reactions following this protocol were tolerant of nitrile, ketone, carboxylic acid, amide, protected and free amino groups, and aromatic hydroxyl groups (Table 6, entries 1–4 and 6–8). These reactions occurred in good to excellent yield with 0.10 to 2.0 mol% catalyst. Even 1-chloro-2-fluorobenzene coupled with thiophenol in excellent yield without a competitive background reaction at the C–F bond. However, both the uncatalyzed and catalyzed reactions of 2-chlorobenzonitrile furnished the corresponding sulfide in good yield (Table 6, entries 10–11).

For reasons we do not understand, the coupling of aromatic thiols conducted with the weaker carbonate base were unsuccessful. As a result, the coupling of aromatic thiols did not occur in the presence of aldehyde groups, and reactions with methyl 3-chlorobenzoate formed 80% of the desired sulfide with 10–15% of the product from transesterification (Table 6, entry 5).

[CyPF-*t*Bu)$PdCl_2$] as catalyst precursor: These data revealed that an equimolecular combination of metal to ligand is adequate to promote the coupling of chloroarenes with both aliphatic and aromatic thiols. Thus, a palladium complex containing a single CyPF-*t*Bu ligand would be an alternative catalyst precursor for the C–S bond-forming reactions. The use of such a compound would alleviate the need to generate the metal–ligand complex in situ. As expected, [(CyPF-*t*Bu)$PdCl_2$] forms in high yield from [$(CH_3CN)_2PdCl_2$] and Josiphos ligand **1** (Scheme 3). Studies

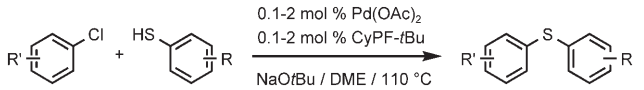


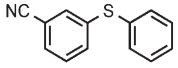
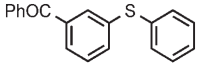
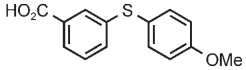
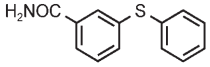
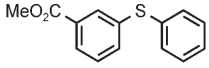
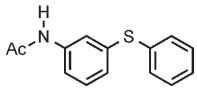
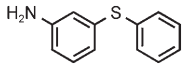
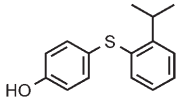
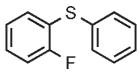
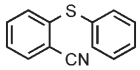
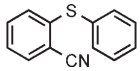
Scheme 3. Synthesis of [(CyPF-*t*Bu)$PdCl_2$].

on reactions catalyzed by this complex are presented in this section. We studied reactions of this compound because it is more stable over the long-term than the complex formed from ligand **1** and $Pd(OAc)_2$.

Representative experiments were performed with the new Pd^{II} complex using the combination of solvent and base developed for the different thiols. As shown in Table 7, the

Table 6. Palladium-catalyzed coupling of functionalized aryl chlorides with aryl thiols using CyPF-*t*Bu ligand.[a]



Entry	Cat. [mol%]	Yield [%][b]	Product
1[c]	0.1	93	
2[c]	0.1	95	
3	0.25	74	
4	0.25	70	
5[d,e]	0.25	80	
6	0.25	99	
7	0.25	91	
8	2.0	91	
9[d]	1.0	96	
10[c]	0.25	99	
11[c,f]	–	87	

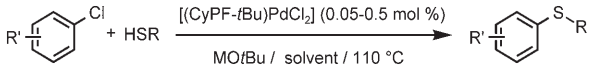
[a] All experiments were conducted with a 1:1 ratio of metal to ligand, 1 mmol of both ArCl and thiol, and 2.4 equiv NaO*t*Bu, unless otherwise stated, in DME (1.5 mL), requiring 2–5 h of heating at 110°C to complete. [b] Isolated yield. [c] 1.1 equiv NaO*t*Bu were employed. [d] Reaction performed using 1.1 equiv KO*t*Bu and toluene as solvent. [e] 10–15% transesterification compound were also isolated. [f] No catalyzed reaction.

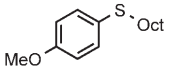
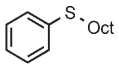
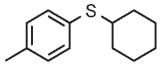
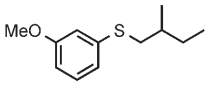
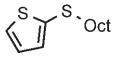
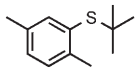
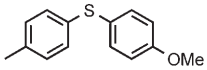
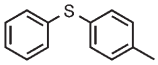
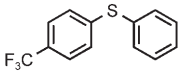
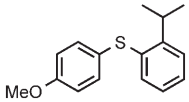
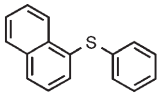
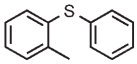
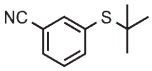
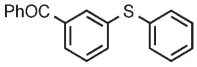
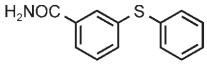
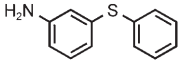
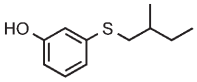
yields, reaction times and catalyst loadings for the coupling of aliphatic thiols catalyzed by [(CyPF-*t*Bu)$PdCl_2$] were comparable to those catalyzed by the combination of $Pd(OAc)_2$ and ligand **1** (Table 7, entries 1–3, 5–6 vs Table 3, entries 1, 3, 14, 16, 21). The reaction of aromatic thiols catalyzed by [(CyPF-*t*Bu)$PdCl_2$] was also efficient (Table 7, entries 7–12). Only one example in this set of reactions required a slight increase in the catalyst loading (0.25 mol% for Table 7, entry 7 vs 0.10 mol% for Table 4, entry 7). Reactions catalyzed by [(CyPF-*t*Bu)$PdCl_2$] also occurred with remarkable functional group tolerance. For instance, reactions of aryl chlorides bearing nitrile, ketone, amide and free amino and aromatic hydroxyl groups occurred in high yields under conditions similar to those of the couplings catalyzed by $Pd(OAc)_2$ and ligand **1** (Table 7, entries 13–17).

Conclusion

In summary, we have shown that palladium complexes generated from the Josiphos ligand CyPF-*t*Bu are general, highly efficient catalysts for the coupling of chloroarenes with thiols. Reactions catalyzed by the complexes generated in situ from $Pd(OAc)_2$ or $[Pd(dba)_2]$ and ligand **1** and reactions catalyzed by $[(CyPF\text{-}tBu)PdCl_2]$ occur with turnover numbers that are typically two orders of magnitude higher than those of related couplings by previous catalysts. The ability to conduct reactions with low catalyst loadings illustrates that the CyPF-*t*Bu ligand resists deactivation processes that could occur by displacement of dative ligands with thiolates. The process exhibits a broad scope and a high tolerance for functionality, such as fluoro, cyano, keto, free carboxylate, amido, carboalkoxy, carboxaldehyde, aromatic and aliphatic hydroxyl and amino functionalities. Only reactions of hindered aryl chlorides with aromatic thiols and reactions of aromatic thiols with chloroarenes containing carboxaldehyde functionality proceed to partial conversion or form significant amounts of side products. Related thiations of more reactive bromo- and iodoarenes, which overcome these few limitations of the reactions of chloroarenes, as well as studies of the mechanism of the coupling process are in progress.

Table 7. Palladium-catalyzed coupling of aryl chlorides with thiols using $[(CyPF\text{-}tBu)PdCl_2]$ complex.[a]



Entry	Cat. [mol %]	Yield [%][b]	Product
1	0.1	97	
2	0.05	97	
3	0.05	94	
4	0.05	98	
5	0.05	93	
6	0.5	96	
7	0.25	88	
8[c]	0.25	97	
9	0.5	90	
10	0.25	94	
11	0.1	98	
12[d]	0.5	77	
13	0.05	91	
14	0.1	80	
15[e]	0.5	66	
16[e]	0.5	92	
17[e]	0.5	96	

[a] Experiments were conducted with 1 mmol of both ArCl and thiol, and 1.1 equiv NaO*t*Bu at 110 °C in DME (1.5 mL). Reactions with unfunctionalized chloroarenes were carried out in toluene (1.5 mL) in the presence of 1.1 equiv KO*t*Bu. [b] Isolated yield. [c] Reaction performed using 1.1 equiv LiHMDS. [d] 18 % symmetrical sulfides were also observed. [e] 2.4 equiv NaO*t*Bu were employed.

Experimental Section

General considerations: All reactions were assembled under an inert atmosphere. Reactions were conducted in 4 mL vials sealed with a cap containing a PTFE septum. All glassware was oven-dried, evacuated and purged with nitrogen immediately prior to use. All reaction temperatures refer to bath temperatures. All common reagents as well as $Pd(OAc)_2$ and bisphosphine ligands **7**–**12** were obtained from commercial suppliers and used without further purification. CyPF-*t*Bu (1-dicyclohexylphosphino-2-di-*tert*-butylphosphinoethylferroceno) as well as the other commercial available Josiphos-type ligands **3**–**6** were obtained from Solvias AG and Strem Chemicals and used without purification. $[Pd(dba)_2]$ was prepared according to literature procedures.[42] Toluene was degassed by purging with nitrogen for 45 min and dried with a solvent purification system containing a 1 m column of activated alumina. 1,2-Dimethoxyethane (DME, 99.9 % purity, HPLC grade) was used without further purification, but was stored under nitrogen. Other solvents were dried by standard methods. Reactions performed at 110 °C in DME (b.p. 85 °C) were conducted using the standard vials and caps cited above; no loss of solvent was observed. ^1H, ^{13}C and $^{31}P\{^1H\}$ NMR spectra were recorded in $CDCl_3$ on 400 MHz or 500 MHz spectrometers with tetramethylsilane or residual protiated solvent used as a reference. Abbreviations for ^1H NMR splitting patterns are: s, singlet; brs, broad singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; sept, septet; oct, octet; dd, doublet of doublets; dt, doublet of triplets; td, triplet of doublets; tt, triplet of triplets; m, multiplet. The coupling constants are reported in Hertz (Hz). Flash column chromatography was carried out on silica gel (230–240 mesh). The yields of the coupled products included in all tables refer to isolated yields and are the average of two runs. Products that had been reported previously were isolated in greater than 95 % purity, as determined by ^1H NMR spectroscopy and capillary gas chromatography (GC). GC analyses were obtained with a DB-1301 narrow bore column suitable for use with a fast temperature ramp (max 120 °C min^{-1}). Elemental Analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia 30071.

Synthesis of Josiphos type ligand 2 (1-dicyclohexylphosphino-2-di-*tert*-butylphosphinomethylferroceno): This bisphosphine was prepared according to literature procedures for related ferrocenyl ligands.[43] Yellow solid (95 % yield); ^1H NMR (CD_2Cl_2): $\delta = 4.67$ (brs, 1H), 4.16 (m, 1H), 4.10 (s, 5H), 4.09–4.05 (m, 1H), 2.70 (m, 2H), 2.28–2.22 (m, 1H), 2.14–2.05 (m,

2H), 1.87–1.60 (m, 13H), 1.47–1.36 (m, 4H), 1.27–1.01 (m, 2H), 1.21 (d, $J=10.8$ Hz, 9H), 1.07 (d, $J=10.8$ Hz, 9H); $^{31}P\{^1H\}$ NMR (CD_2Cl_2): $\delta=$ 26.0 (s), 11.8 (s); elemental analysis calcd (%) for $C_{31}H_{50}P_2Fe$: C 68.88, H 9.32; found: C 68.85, H 9.47.

Preparation of stock solution A (1.0×10^{-2} M): DME (1.0 mL) was added to a mixture of $Pd(OAc)_2$ (2.2 mg) and CyPF-*t*Bu (5.5 mg). The resulting orange solution was stirred at room temperature for 1 min prior to subsequent reactions.

General procedure for the palladium-catalyzed coupling of aryl chlorides with aliphatic thiols: The appropriate quantity of stock solution A was added to a 4 mL vial containing the aryl chloride (1.00 mmol) and sodium *tert*-butoxide (106 mg, 1.10 mmol) in DME (1.5 mL). The aliphatic thiol (1.00 mmol) was then added, and the vial sealed with a cap containing a PTFE septum. The mixture was heated at 110 °C until the chloroarene was consumed, as determined by GC. Silica gel (0.5 g) was added, and the solvents were evaporated under reduced pressure. The crude residue was purified by column chromatography on silica gel using hexane or a mixture of hexane and ethyl acetate as eluent. Aryl sulfides were isolated in the yields reported in Table 3.

4-Methoxyphenyl octyl sulfide (Table 3, entry 1):[33] 100 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (98% yield). ^1H NMR ($CDCl_3$): $\delta=7.25$ (d, $J=8.6$ Hz, 2H), 6.76 (d, $J=8.6$ Hz, 2H), 3.71 (s, 3H), 2.73 (t, $J=7.4$ Hz, 2H), 1.50 (quint, $J=7.4$ Hz, 2H), 1.30 (quint, $J=7.4$ Hz, 2H), 1.22–1.14 (m, 8H), 0.80 (t, $J=7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=158.6$, 132.8 (2C), 126.9, 114.4 (2C), 55.2, 35.7, 31.7, 29.3, 29.09, 29.06, 28.6, 22.6, 14.0.

Octyl phenyl sulfide (Table 3, entry 2):[44] 100 μL of stock solution A were used; column chromatography: hexane; colorless liquid (91% yield). ^1H NMR ($CDCl_3$): $\delta=7.25$–7.23 (m, 2H), 7.21–7.16 (m, 2H), 7.09–7.06 (m, 1H), 2.83 (t, $J=7.4$ Hz, 2H), 1.57 (quint, $J=7.4$ Hz, 2H), 1.34 (quint, $J=7.4$ Hz, 2H), 1.21–1.18 (m, 8H), 0.80 (t, $J=7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 137.0, 128.7 (4C), 125.5, 33.5, 31.7, 29.09, 29.06 (2C), 28.8, 22.6, 14.0.

Octyl phenyl sulfide (Table 3, entry 3): 50 μL of stock solution A were used; colorless liquid (91% yield).

Octyl phenyl sulfide (Table 3, entry 4): 10 μL of stock solution A were used; colorless liquid (85% yield).

Preparation of stock solution B (1.0×10^{-2} M): $Pd(OAc)_2$ (2.2 mg) and CyPF-*t*Bu (5.5 mg) were added in air to a 4 mL vial. The flask was sealed with a cap containing a PTFE septum and then evacuated and backfilled with N_2. DME (1.0 mL) was then added to the vial by syringe, and the resulting orange solution was stirred at room temperature for 1 min prior to subsequent reactions.

Representative procedure without using a drybox

A) 1 mmol scale (Table 3, entry 5): An oven-dried test tube with a screw cap containing a PTFE-lined septum was evacuated and backfilled with N_2. To the flask was added NaO*t*Bu (106 mg, 1.10 mmol) and a stir bar. The flask was evacuated and heated to remove the moisture present in the base; then evacuated and backfilled with N_2 three times. To the flask was then added chlorobenzene (102 μL, 1.00 mmol), DME (2.0 mL), 50 μL of stock solution B, and 1-octanethiol (173 μL, 1.00 mmol), which were stored and handled under an inert atmosphere. The resulting mixture was stirred for 6 h at 110 °C until the chlorobenzene was consumed, as determined by GC. Silica gel (0.5 g) was then added, and solvents were evaporated under reduced pressure. The crude residue was purified by column chromatography on silica gel using hexane as eluent to give octyl phenyl sulfide as a colorless liquid (205 mg, 92%).

B) 5 mmol scale (Table 3, entry 6): NaO*t*Bu (0.53 g, 5.50 mmol), chlorobenzene (0.51 mL, 5.00 mmol), DME (10.0 mL), 250 μL of stock solution B, and 1-octanethiol (0.87 mL, 5.00 mmol) were used following the same procedure described above to give, after 18 h, octyl phenyl sulfide as a colorless liquid (1.03 g, 93%).

4-Methylphenyl octyl sulfide (Table 3, entry 7):[33] 50 μL of stock solution A were used. Column chromatography: hexane, then hexane/ethyl acetate 50:1; colorless liquid (97% yield). ^1H NMR ($CDCl_3$): $\delta?=7.10$ (d, $J=8.1$ Hz, 2H), 6.95 (d, $J=8.1$ Hz, 2H), 2.73 (t, $J=7.4$ Hz, 2H), 2.17 (s, 3H), 1.48 (quint, $J=7.4$ Hz, 2H), 1.26 (quint, $J=7.4$ Hz, 2H), 1.17–1.08 (m, 8H), 0.74 (t, $J=6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=135.7$, 133.1, 129.7 (2C), 129.5 (2C), 34.3, 31.7, 29.2, 29.10, 29.06, 28.7, 22.6, 20.9, 14.0.

4-Methylphenyl octyl sulfide (Table 3, entry 8): A solution of $Pd(OAc)_2$ (4.4 mg) and CyPF-*t*Bu (11 mg) in DME (1 mL) was used as catalyst; the reaction was conducted at 70 °C; 97% yield.

2-Methylbutyl phenyl sulfide (Table 3, entry 9):[45] 50 μL of stock solution **A** were used; column chromatography: hexane; colorless liquid (95% yield). ^1H NMR ($CDCl_3$): $\delta=7.25$–7.22 (m, 2H), 7.20–7.15 (m, 2H), 7.08–7.04 (m, 1H), 2.86 (dd, $J=6.0$, 12.6 Hz, 1H), 2.66 (dd, $J=7.6$, 12.6 Hz, 1H), 1.57 (m, 1H), 1.45 (m, 1H), 1.18 (m, 1H), 0.94 (d, $J=6.6$ Hz, 3H), 0.82 (t, $J=7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=137.5$, 128.7 (2C), 128.6 (2C), 125.4, 40.6, 34.4, 28.7, 18.8, 11.2.

1-Methylpropyl phenyl sulfide (Table 3, entry 10):[44] 50 μL of stock solution **A** were used; column chromatography: hexane; colorless liquid (91% yield). ^1H NMR ($CDCl_3$): $\delta=7.32$–7.29 (m, 2H), 7.20–7.16 (m, 2H), 7.13–7.09 (m, 1H), 3.07 (sext, $J=6.6$ Hz, 1H), 1.57 (m, 1H), 1.45 (m, 1H), 1.18 (d, $J=6.6$ Hz, 3H), 0.92 (t, $J=7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=135.4$, 131.7 (2C), 128.6 (2C), 126.4, 44.7, 29.4, 20.4, 11.4.

1-Methylpropyl phenyl sulfide (Table 3, entry 11): A solution of $Pd(OAc)_2$ (4.4 mg) and CyPF-*t*Bu (11 mg) in DME (1 mL) was used as catalyst; the reaction was conducted at 70 °C; 89% yield.

2-Methyl-2-propyl 4-trifluoromethylphenyl sulfide (Table 3, entry 12): 100 μL of stock solution A were used; column chromatography: hexane; colorless liquid (82% yield). ^1H NMR ($CDCl_3$): $\delta=7.56$ (d, $J=7.9$ Hz, 2H), 7.50 (d, $J=7.9$ Hz, 2H), 1.23 (s, 9H); ^{13}C NMR ($CDCl_3$): $\delta=137.6$, 137.3 (2C), 130.5 (q, $^2J_{C,F}=32.6$ Hz), 125.2 (q, $^3J_{C,F}=3.8$ Hz), 124.5 (q, $^1J_{C,F}=272.5$ Hz), 46.6, 30.9 (3C); elemental analysis calcd (%) for $C_{11}H_{13}F_3S$: C 56.39, H 5.59; found: C 56.59, H 5.60.

1-Naphthalenyl octyl sulfide (Table 3, entry 13):[46] 50 μL of stock solution A were used; column chromatography: hexane; colorless liquid (92% yield). ^1H NMR ($CDCl_3$): $\delta=8.45$ (d, $J=8.8$ Hz, 1H), 7.86 (d, $J=8.2$ Hz, 1H), 7.74 (d, $J=8.2$ Hz, 1H), 7.60–7.52 (m, 3H), 7.43 (t, $J=8.2$ Hz, 1H), 3.0 (t, $J=7.5$ Hz, 2H), 1.71 (quint, $J=7.5$ Hz, 2H), 1.49–1.45 (m, 2H), 1.30 (br s, 8H), 0.92 (t, $J=7.6$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=134.2$, 133.8, 132.8, 128.4, 127.3, 126.7, 126.1, 126.0, 125.5, 124.9, 34.1, 31.7, 29.1 (3C), 28.8, 22.6, 14.0.

Octyl 2-thiophenyl sulfide (Table 3, entry 14):[47] 50 μL of stock solution **A** were used; column chromatography: hexan; colorless liquid (96% yield). ^1H NMR ($CDCl_3$): $\delta=7.23$ (dd, $J=5.4$, 1.3 Hz, 1H), 7.02 (dd, $J=3.5$, 1.3 Hz, 1H), 6.88 (dd, $J=5.4$, 3.5 Hz, 1H), 2.70 (t, $J=7.3$ Hz, 2H), 1.53 (quint, $J=7.3$ Hz, 2H), 1.33–1.27 (m, 2H), 1.20 (br s, 8H), 0.80 (t, $J=6.9$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=134.9$, 133.1, 128.7, 127.3, 38.9, 31.7, 29.3, 29.1, 29.0, 28.3, 22.6, 14.0.

Cyclohexyl 3-methylphenyl sulfide (Table 3, entry 15):[48] 50 μL of stock solution A were used; column chromatography: hexane, then hexane/ethyl acetate 50:1; colorless liquid (98% yield). ^1H NMR ($CDCl_3$): $\delta=$ 7.14–7.07 (m, 3H), 6.95–6.93 (m, 1H), 3.02 (tt, $J=10.4$, 3.7 Hz, 1H), 2.24 (s, 3H), 1.92–1.89 (m, 2H), 1.71–1.67 (m, 2H), 1.55–1.51 (m, 1H), 1.33–1.13 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta=138.4$, 134.8, 132.4, 128.8, 128.5, 127.4, 46.4, 33.3 (2C), 26.0, 25.7 (2C), 21.2.

Cyclohexyl 4-methylphenyl sulfide (Table 3, entry 16):[48] 50 μL of stock solution A were used. ; column chromatography: hexane, then hexane/ethyl acetate 50:1; colorless liquid (97% yield). ^1H NMR ($CDCl_3$): $\delta=$ 7.23 (d, $J=8.0$ Hz, 2H), 7.01 (d, $J=8.0$ Hz, 2H), 2.93 (tt, $J=10.5$, 3.8 Hz, 1H), 2.24 (s, 3H), 1.89–1.86 (m, 2H), 1.69–1.66 (m, 2H), 1.53–1.49 (m, 1H), 1.30–1.11 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta=136.7$, 132.7 (2C), 131.1, 129.4 (2C), 47.0, 33.3 (2C), 26.0, 25.7 (2C), 21.0.

Cyclohexyl 4-methylphenyl sulfide (Table 3, entry 17): A solution of $Pd(OAc)_2$ (4.4 mg) and CyPF-*t*Bu (11 mg) in DME (1 mL) was used as catalyst; the reaction was conducted at 70 °C; 91% yield.

Cyclohexyl 2-methylphenyl sulfide (Table 3, entry 18):[48] 250 μL of stock solution **A** were used; column chromatography: hexan; colorless liquid (90% yield). ^1H NMR ($CDCl_3$): $\delta=7.41$–7.39 (m, 1H), 7.22–7.20 (m, 1H), 7.18–7.13 (m, 2H), 3.12 (tt, $J=10.4$, 3.7 Hz, 1H), 2.43 (s, 3H), 2.02–2.00 (m, 2H), 1.82–1.79 (m, 2H), 1.66–1.64 (m, 1H), 1.47–1.28 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta=139.3$, 134.5, 131.2, 130.1, 126.3, 126.1, 45.8, 33.3 (2C), 26.0, 25.7 (2C), 20.7.

2-Methylphenyl octyl sulfide (Table 3, entry 19): 250 μL of stock solution A were used; column chromatography: hexane; colorless liquid (95% yield). ^{1}H NMR ($CDCl_3$): δ = 7.15 (d, J = 8.2 Hz, 1H), 7.06–7.03 (m, 2H), 6.98–6.95 (m, 1H), 2.79 (t, J = 7.4 Hz, 2H), 2.27 (s, 3H), 1.57 (quint, J = 7.5 Hz, 2H), 1.38–1.32 (m, 2H), 1.19 (brs, 8H), 0.80 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 137.0, 136.4, 129.9, 127.1, 126.2, 125.1, 32.7, 31.7, 29.1 (2C), 28.9 (2C), 22.6, 20.2, 14.0; elemental analysis calcd (%) for $C_{15}H_{24}S$: C 76.20, H 10.23; found: C 76.41, H 10.17.

2-Methoxyphenyl octyl sulfide (Table 3, entry 20): 250 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (97% yield). ^{1}H NMR ($CDCl_3$): δ = 7.23 (dd, J = 7.6, 1.6 Hz, 1H), 7.15–7.12 (m, 1H), 6.90 (td, J = 7.6, 1.3 Hz, 1H), 6.82 (dd, J = 8.0, 1.3 Hz, 1H), 3.86 (s, 3H), 2.87 (t, J = 7.6 Hz, 2H), 1.65 (quint, J = 7.6 Hz, 2H), 1.43 (m, 2H), 1.31–1.22 (m, 8H), 0.87 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 156.9, 128.4, 126.4, 125.1, 120.8, 110.1, 55.5, 31.7, 31.6, 29.0 (2C), 28.8, 28.7, 22.5, 13.9; elemental analysis calcd (%) for $C_{22}H_{31}O_2S$: C 73.49, H 8.69; found: C 73.76, H 8.82.

2,5-Dimethylphenyl 2-methyl-2-propyl sulfide (Table 3, entry 21):[25] 500 μL of stock solution A were used; column chromatography: hexane; colorless liquid (89% yield). ^{1}H NMR ($CDCl_3$): δ = 7.26 (s, 1H), 7.06 (d, J = 7.9 Hz, 1H), 6.96 (d, J = 7.9 Hz, 1H), 2.38 (s, 3H), 2.21 (s, 3H), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 140.5, 139.4, 135.0, 131.7, 130.0, 129.6, 46.9, 31.0 (3C), 21.2, 20.6.

2,6-Dimethylphenyl 2-methyl-2-propyl sulfide (Table 3, entry 22):[25] A solution of $Pd(OAc)_2$ (6.6 mg) and CyPF-*t*Bu (16.5 mg) in DME (1 mL) was used as catalyst; column chromatography: hexane; colorless liquid (77% yield; 82% conversion after 36 h of reaction). ^{1}H NMR ($CDCl_3$): δ = 7.04 (brs, 3H), 2.49 (s, 6H), 1.21 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 145.2 (2C), 132.1, 128.2, 127.9 (2C), 49.1, 31.5 (3C), 23.0 (2C).

Preparation of stock solution C (1.0×10^{-2} M): Toluene (1.0 mL) was added to a mixture of $[Pd(dba)_2]$ (2.2 mg) and CyPF-*t*Bu (5.5 mg). The resulting purple solution was stirred at room temperature for 1 min prior to subsequent reactions.

General procedure for the palladium-catalyzed coupling of aryl chlorides with aromatic thiols: The appropriate quantity of stock solution C was added to a 4 mL vial containing the aryl chloride (1.00 mmol) and potasium *tert*-butoxide (123 mg, 1.10 mmol) in toluene (1.5 mL). The aromatic thiol (1.00 mmol) was then added, and the vial sealed with a cap containing a PTFE septum. The mixture was heated at 110°C until the chloroarene was consumed, as determined by GC. Silica gel (0.5 g) was then added, and solvents were evaporated under reduced pressure. The crude residue was purified by column chromatography on silica gel using hexane or a mixture of hexane and ethyl acetate as eluent. Aryl sulfides were isolated in the yields reported in Table 4.

4-Methoxyphenyl phenyl sulfide (Table 4, entry 1):[49] 100 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (98% yield). ^{1}H NMR ($CDCl_3$): δ = 7.23 (d, J = 8.8 Hz, 2H), 7.06–7.02 (m, 2H), 7.00–6.93 (m, 3H), 6.71 (d, J = 8.8 Hz, 2H), 3.62 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.7, 138.5, 135.3 (2C), 128.8 (2C), 128.1 (2C), 125.7, 124.2, 114.9 (2C), 55.3.

Diphenyl sulfide (Table 4, entry 2):[49] 100 μL of stock solution C were used; column chromatography: hexane; colorless liquid (95% yield). ^{1}H NMR ($CDCl_3$): δ = 7.26–7.24 (m, 4H), 7.21–7.18 (m, 4H), 7.16–7.13 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 135.7 (2C), 130.9 (4C), 129.1 (4C), 126.9 (2C).

4-Methylphenyl phenyl sulfide (Table 4, entry 3):[49] 100 μL of stock solution C were used; column chromatography: hexane; colorless liquid (95% yield). ^{1}H NMR ($CDCl_3$): δ = 7.21 (d, J = 8.0 Hz, 2H), 7.19–7.14 (m, 4H), 7.11–7.05 (m, 1H), 7.03 (d, J = 8.0 Hz, 2H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 137.5, 137.0, 132.2 (2C), 131.2, 130.0 (2C), 129.7 (2C), 128.9 (2C), 126.3, 21.0.

4-Methylphenyl phenyl sulfide (Table 4, entry 4): A solution of $[Pd(dba)_2]$ (6.6 mg) and CyPF-*t*Bu (16.5 mg) in toluene (1.0 mL) was used as catalyst; the reaction was heated at 70°C until no further reaction was observed (93% conversion); 83% yield.

3-Methylphenyl phenyl sulfide (Table 4, entry 5):[50] 100 μL of stock solution C were used; column chromatography: hexane; colorless liquid (98% yield). ^{1}H NMR ($CDCl_3$): δ = 7.22–7.20 (m, 2H), 7.17–7.14 (m, 2H), 7.11–7.03 (m, 4H), 6.92 (m, 1H), 2.18 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 138.9, 136.0, 135.1, 131.7, 130.6 (2C), 129.0 (2C), 128.9, 128.2, 127.9, 126.7, 21.2.

3-Methylphenyl phenyl sulfide (Table 4, entry 6): 50 μL of stock solution C were used; 86% yield.

4-Methylphenyl 4-methoxyphenyl sulfide (Table 4, entry 7):[51] 100 μL of stock solution C were used; column chromatography hexane/ethyl acetate 50:1; white solid (95% yield). ^{1}H NMR ($CDCl_3$): δ = 7.47 (d, J = 8.8 Hz, 2H), 7.25 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.3, 135.9, 134.21 (2C), 134.15, 129.6 (2C), 129.2 (2C), 125.4, 114.7 (2C), 55.1, 20.8.

3-Methylphenyl 4-methylphenyl sulfide (Table 4, entry 8):[52] 100 μL of stock solution C and LiHMDS (184 mg, 1.10 mmol) were used; column chromatography; hexane; colorless liquid (93% yield). ^{1}H NMR ($CDCl_3$): δ = 7.28–7.25 (m, 2H), 7.16–7.07 (m, 5H), 6.97 (d, J = 7.3 Hz, 1H), 2.31 (s, 3H), 2.26 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 138.7, 137.2, 136.5, 131.9 (2C), 131.5, 130.5, 129.9 (2C), 128.8, 127.3, 127.0, 21.2, 21.0.

4-Methylphenyl phenyl sulfide (Table 4, entry 9): 250 μL of stock solution C and LiHMDS (184 mg, 1.10 mmol) were used; column chromatography: hexane; colorless liquid (98% yield). ^{1}H NMR ($CDCl_3$): δ = 7.21 (d, J = 8.0 Hz, 2H), 7.19–7.14 (m, 4H), 7.11–7.05 (m, 1H), 7.03 (d, J = 8.0 Hz, 2H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 137.5, 137.0, 132.2 (2C), 131.2, 130.0 (2C), 129.7 (2C), 128.9 (2C), 126.3, 21.0.

Di-4-methoxyphenyl sulfide (Table 4, entry 10):[28] 250 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1;: white solid (99% yield). ^{1}H NMR ($CDCl_3$): δ = 7.26 (d, J = 8.8 Hz, 4H), 6.81 (d, J = 8.8 Hz, 4H), 3.76 (s, 6H); ^{13}C NMR ($CDCl_3$): δ = 158.8 (2C), 132.6 (4C), 127.3 (2C), 114.6 (4C), 55.2 (2C).

3-Methylphenyl 4-methoxyphenyl sulfide (Table 4, entry 11): 250 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (97% yield). ^{1}H NMR ($CDCl_3$): δ = 7.38 (d, J = 8.8 Hz, 2H), 7.09 (t, J = 7.8 Hz, 1H), 7.01 (s, 1H), 6.96–6.91 (m, 2H), 6.85 (d, J = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 159.6, 138.6, 138.1, 135.0 (2C), 128.8, 128.7, 126.6, 125.3, 124.4, 114.8 (2C), 55.1, 21.2; elemental analysis calcd (%) for $C_{14}H_{14}OS$: C 73.01, H 6.13; found: C 73.27, H 6.57.

Phenyl 4-trifluoromethylphenyl sulfide (Table 4, entry 12):[53] 500 μL of stock solution C were used; column chromatography: hexane; colorless liquid (89% yield). ^{1}H NMR ($CDCl_3$): δ = 7.47–7.45 (m, 4H), 7.39–7.35 (m, 3H), 7.28–7.24 (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 142.8, 133.5 (2C), 132.4, 129.6 (2C), 128.6, 128.2 (2C), 128.1 (q, $^2J_{C,F}$ = 32.6 Hz), 125.7 (d, $^3J_{C,F}$ = 3.8 Hz), 124.0 (q, $^1J_{C,F}$ = 271.6 Hz).

2-Isopropylphenyl 4-methoxyphenyl sulfide (Table 4, entry 13):[54] 250 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1; white solid (94% yield). ^{1}H NMR ($CDCl_3$): δ = 7.44 (d, J = 8.8 Hz, 2H), 7.41 (d, J = 7.8 Hz, 1H), 7.31–7.27 (m, 1H), 7.17–7.13 (m, 2H), 6.99 (d, J = 8.8 Hz, 2H), 3.88 (s, 3H), 3.68 (sept, J = 6.9 Hz, 1H), 1.38 (d, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 159.2, 147.5, 135.6, 134.2 (2C), 130.0, 126.6, 126.2, 125.4, 125.3, 114.8 (2C), 55.1, 30.2, 23.2 (2C).

2-Isopropylphenyl 4-methylphenyl sulfide (Table 4, entry 14): 250 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (97% yield). ^{1}H NMR ($CDCl_3$): δ = 7.32 (dd, J = 7.7, 1.4 Hz, 1H), 7.26–7.14 (m, 4H), 7.11–7.06 (m, 3H), 3.54 (sept, J = 6.8 Hz, 1H), 2.32 (s, 3H), 1.22 (d, J = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 149.2, 136.4, 133.8, 132.7, 132.3, 130.6 (2C), 129.8 (2C), 127.6, 126.4, 125.7, 30.4, 23.4 (2C), 20.9, elemental analysis calcd (%) for $C_{16}H_{18}S$: C 79.29, H 7.49; found: C 78.99, H 7.57.

1-Naphthalenyl phenyl sulfide (Table 4, entry 15):[46] 100 μL of stock solution C were used; column chromatography hexane/ethyl acetate 50:1; colorless liquid (84% yield); 10% of symmetrical sulfides were also formed. ^{1}H NMR ($CDCl_3$): δ = 8.26 (s, 1H), 7.71–7.53 (m, 3H), 7.37–7.0 (m, 8H); ^{13}C NMR ($CDCl_3$): δ = 136.8, 134.1, 133.5, 132.4, 131.1, 129.1, 129.0 (2C), 128.9 (2C), 128.5, 126.8, 126.3, 126.0, 125.7, 125.5.

1-Naphthalenyl phenyl sulfide (Table 4, entry 16): A solution of $[Pd(dba)_2]$ (6.6 mg) and CyPF-*t*Bu (16.5 mg) in toluene (1.0 mL) was used as

catalyst; the reaction was heated at 90 °C until reaction was complete (48 h); 95 % yield.

2,5-Dimethylphenyl 4-methoxyphenyl sulfide (Table 4, entry 17):[25] 1000 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1 → 20:1; colorless liquid (92 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.27 (d, J = 8.8 Hz, 2H), 7.03 (d, J = 7.6 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 6.86–6.82 (m, 3H), 3.75 (s, 3H), 2.31 (s, 3H), 2.18 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 159.2, 136.1, 135.9, 134.3, 133.8 (2C), 130.1, 130.0, 127.1, 124.9, 114.8 (2C), 55.1, 20.8, 19.7.

2-Methoxyphenyl phenyl sulfide (Table 4, entry 18):[49] 1000 μL of stock solution C were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (97 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.42–7.40 (m, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.32–7.27 (m, 2H), 7.14 (dt, J = 7.8, 1.7 Hz, 1H), 6.96–6.90 (m, 2H), 3.91 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 157.1, 134.3, 131.4, 131.3 (2C), 129.0 (2C), 128.2, 126.9, 123.9, 121.1, 110.7, 55.7.

2-Methylphenyl phenyl sulfide (Table 4, entry 19):[49] 500 μL of stock solution C were used; column chromatography: hexane; colorless liquid (70 % yield); ~20 % of symmetrical sulfides were also formed. ^{1}H NMR ($CDCl_3$): δ = 7.47–7.19 (m, 9H), 2.50 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 136.0, 133.6, 132.9, 130.9, 130.5, 129.5 (2C), 129.0 (2C), 127.8, 126.6, 126.2, 20.5.

2-Isopropylphenyl 2-methylphenyl sulfide (Table 4, entry 20):[54] 250 μL of stock solution C were used; column chromatography: hexane; colorless liquid (70 % yield); ~20 % of symmetrical sulfides were also formed. ^{1}H NMR ($CDCl_3$): δ = 7.26 (d, J = 7.6 Hz, 1H), 7.19–7.14 (m, 2H), 7.07 (t, J = 7.3 Hz, 1H), 7.02–6.99 (m, 3H), 6.95 (d, J = 7.6 Hz, 1H), 3.43 (sept, J = 6.7 Hz, 1H), 2.31 (s, 3H), 1.17 (d, J = 6.7 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 149.3, 138.3, 135.3, 132.9, 131.9, 130.9, 130.3, 127.6, 126.7, 126.54, 126.49, 125.8, 30.5, 23.4 (2C), 20.3.

General procedure for the palladium-catalyzed coupling of functionalized aryl chlorides with aliphatic and aromatic thiols: The appropriate quantity of stock solution A was added to a 4 mL vial containing the aryl chloride (1.00 mmol) and NaO*t*Bu (230 mg, 2.40 mmol), unless otherwise stated, in DME (1.5 mL). The thiol (1.00 mmol) was then added, and the vial sealed with a cap containing a PTFE septum. The mixture was heated at 110 °C until the chloroarene was consumed, as determined by GC. Silica gel (0.5 g) was added, and the solvents were evaporated under reduced pressure. The crude residue was purified by column chromatography on silica gel using hexane or mixtures of hexane and ethyl acetate as eluent. Aryl sulfides were isolated in the yields reported in Tables 5 and 6.

3-Cyanophenyl 2-methyl-2-propyl sulfide (Table 5, entry 1): 50 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 50:1; white solid (90 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.82 (s, 1H), 7.76 (d, J = 7.8 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.8 Hz, 1H), 1.30 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 141.5, 140.2, 134.7, 132.0, 129.1, 118.1, 112.6, 46.7, 30.8 (3C); elemental analysis calcd (%) for $C_{11}H_{13}NS$: C 69.07, H 6.85, N 7.32; found: C 69.25, H 6.78, N 7.25.

3-Cyanophenyl 2-methyl-2-propyl sulfide (Table 5, entry 2): 10 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; 79 % yield.

3-Benzoylphenyl cyclohexyl sulfide (Table 5, entry 3): 50 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 50:1, then 20:1; colorless oil (86 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.90–7.78 (m, 3H), 7.62–7.56 (m, 3H), 7.47 (t, J = 7.9 Hz, 2H), 7.38 (t, J = 7.8 Hz, 1H), 3.16 (tt, J = 10.4, 3.7 Hz, 1H), 2.0–1.96 (m, 2H), 1.78–1.75 (m, 2H), 1.62–1.59 (m, 1H), 1.42–1.21 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 195.9, 138.0, 137.2, 136.0, 134.9, 132.4, 132.2, 129.9 (2C), 128.5, 128.1 (2C), 127.8, 46.2, 33.0 (2C), 25.8, 25.5 (2C); elemental analysis calcd (%) for $C_{19}H_{20}OS$: C 76.98, H 6.80; found: C 76.95, H 6.79.

3-(1-Methylpropylsulfanyl)benzoic acid (Table 5, entry 4): 100 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 5:1, then 3:1; pale yellow oil (76 % yield). ^{1}H NMR ($CDCl_3$): δ = 11.92 (brs, 1H), 8.12 (s, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 7.9 Hz, 1H), 7.39 (t, J = 7.9 Hz, 1H), 3.25 (sext, J = 6.6 Hz, 1H), 1.73–1.64 (m, 1H), 1.62–1.53 (m, 1H), 1.31 (d, J = 6.6 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 171.9, 136.8, 136.5, 132.5, 129.8, 128.8, 128.1, 44.7, 29.4, 20.4, 11.3; elemental analysis calcd (%) for $C_{11}H_{14}O_2S$: C 62.83, H 6.71; found: C 62.87, H 6.80.

3-(2-Methyl-2-propylsulfanyl)benzoic acid (Table 5, entry 5):[55] 50 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 5:1, then 3:1; white solid (67 % yield). ^{1}H NMR ($CDCl_3$): δ = 12.01 (brs, 1H), 8.30 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 1.31 (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 171.8, 142.6, 138.7, 133.6, 130.3, 129.6, 128.6, 46.3, 30.9 (3C).

3-(2-Methyl-2-propylsulfanyl)benzoic acid (Table 5, entry 6): 10 μL of stock solution A were used; 71 % yield.

3-(2-Methyl-2-propylsulfanyl)benzamide (Table 5, entry 7): 50 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 1:1 mixture; white solid (98 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.99 (t, J = 1.7 Hz, 1H), 7.85 (dt, J = 7.8, 1.4 Hz, 1H), 7.68 (td, J = 7.8, 1.7 Hz, 1H), 7.41 (t, J = 7.8 Hz, 1H), 6.70–6.48 (m, 2H), 1.29 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 169.2, 140.6, 135.9, 133.7, 133.4, 128.6, 127.7, 46.2, 30.8 (3C); elemental analysis calcd (%) for $C_{11}H_{15}NOS$: C 63.12, H 7.22, N 6.69; found: C 62.92, H 7.19, N 6.57.

3-(2-Methyl-2-propylsulfanyl)benzamide (Table 5, entry 8): 10 μL of stock solution A were used; 91 % yield.

Methyl 3-cyclohexylsulfanylbenzoate (Table 5, entry 9):[25] 100 μL of stock solution A and NaO*t*Bu (98 mg, 1.02 mmol) were used; column chromatography: hexane/ethyl acetate 50:1; pale yellow oil (56 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.97 (s, 1H), 7.78 (d, J = 7.9 Hz, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.28–7.24 (m, 1H), 3.83 (s, 3H), 3.10–3.05 (m, 1H), 1.90–1.86 (m, 2H), 1.69–1.67 (m, 2H), 1.54–1.51 (m, 1H), 1.33–1.15 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 166.5, 136.0, 135.8, 132.3, 130.6, 128.6, 127.5, 52.0, 46.4, 33.1 (2C), 25.8, 25.6 (2C).

Methyl 3-cyclohexylsulfanylbenzoate (Table 5, entry 10): 500 μL of stock solution A and Cs_2CO_3 (359 mg, 1.10 mmol) were used; 72 % yield.

3-(2-Methyl-2-propylsulfanyl)benzaldehyde (Table 5, entry 11): 250 μL of stock solution A and Cs_2CO_3 (359 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 50:1; colorless oil (91 % yield). ^{1}H NMR ($CDCl_3$): δ = 10.03 (s, 1H), 8.02 (t, J = 1.6 Hz, 1H), 7.88 (dt, J = 7.6, 1.6 Hz, 1H), 7.79 (dt, J = 7.6, 1.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 1.31 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 191.5, 143.0, 138.2, 136.5, 134.2, 129.4, 128.9, 46.2, 30.7 (3C); elemental analysis calcd (%) for $C_{11}H_{14}OS$: C 68.00, H 7.26; found: C 67.88, H 7.45.

***N*-(3-(2-Methylbutylsulfanyl)phenyl) acetamide** (Table 5, entry 12): 250 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 3:1, then 1:1; white solid (99 % yield). ^{1}H NMR ($CDCl_3$): δ = 8.45 (brs, 1H), 7.58 (s, 1H), 7.27 (d, J = 7.9 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 7.01 (d, J = 7.9 Hz, 1H), 2.89 (dd, J = 6.0, 12.6 Hz, 1H), 2.70 (dd, J = 7.6, 12.6 Hz, 1H), 2.14 (s, 3H), 1.63 (oct, J = 6.6 Hz, 1H), 1.54–1.46 (m, 1H), 1.27–1.19 (m, 1H), 0.98 (d, J = 6.6 Hz, 3H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 169.0, 138.4, 138.3, 128.9, 123.9, 119.6, 117.0, 40.2, 34.2, 28.5, 24.2, 18.7, 11.0; elemental analysis calcd (%) for $C_{13}H_{19}NOS$: C 65.78, H 8.07, N 5.90; found: C 65.54, H 8.12, N 5.89.

3-(2-Methyl-2-propylsulfanyl)aniline (Table 5, entry 13): 250 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 20:1, then 5:1; yellow oil (96 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.10 (t, J = 7.8 Hz, 1H), 6.93 (d, J = 7.6 Hz, 1H), 6.87 (s, 1H), 6.67 (dd, J = 7.8, 2.5 Hz, 1H), 3.71 (brs, 2H), 1.29 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 146.1, 133.2, 129.0, 127.5, 123.7, 115.4, 45.6, 30.9 (3C); elemental analysis calcd (%) for $C_{10}H_{15}NS$: C 66.25, H 8.34, N 7.73; found: C 66.16, H 8.34, N 7.76.

4-(2-Methyl-2-propylsulfanyl)phenol (Table 5, entry 14):[56] 1000 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 5:1, then 3:1; white solid (91 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.39 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 5.62 (brs, 1H), 1.26 (s, 9H); ^{13}C NMR ($CDCl_3$): δ = 156.3, 139.0 (2C), 123.4, 115.5 (2C), 45.6, 30.6 (3C).

3-(2-Methylbutylsulfanyl)phenol (Table 5, entry 15): 500 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 20:1; yellow oil (85 % yield). ^{1}H NMR ($CDCl_3$): δ = 7.04 (t, J = 7.9 Hz, 1H), 6.80 (m, 1H), 6.72 (t, J = 2.1 Hz, 1H), 6.53 (m, 1H), 5.90–4.20 (brs, 1H),

2.84 (dd, $J=12.3$, 5.7 Hz, 1H), 2.65 (dd, $J=12.3$, 7.6 Hz, 1H), 1.58 (oct, $J=6.6$ Hz, 1H), 1.49–1.40 (m, 1H), 1.22–1.13 (m, 1H), 0.93 (d, $J=6.6$ Hz, 3H), 0.82 (d, $J=7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=155.6$, 139.1, 129.8, 120.7, 115.0, 112.5, 40.2, 34.3, 28.7, 18.8, 11.1; elemental analysis calcd (%) for $C_{11}H_{16}OS$: C 67.30, H 8.22; found: C 67.52, H 8.27.

2-Octylsulfanylphenol (Table 5, entry 16):[57] A solution of $Pd(OAc)_2$ (4.4 mg) and CyPF-*t*Bu (11 mg) in DME (1 mL) as catalyst was used; column chromatography: hexane/ethyl acetate 50:1; yellow liquid (97% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.38$ (dd, $J=7.6$, 1.5 Hz, 1H), 7.17 (dt, $J=7.6$, 1.5 Hz, 1H), 6.90 (d, $J=8.1$ Hz, 1H), 6.80–6.76 (m, 1H), 6.70 (brs, 1H), 2.60 (t, $J=7.5$ Hz, 2H), 1.50–1.43 (m, 2H), 1.31–1.17 (m, 10H), 0.79 (t, $J=6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=156.8$, 135.8, 130.8, 120.6, 119.1, 114.6, 36.7, 31.7, 29.5, 29.04, 28.98, 28.5, 22.5, 14.0.

4-(1-Hydroxyethyl)phenyl 2-methyl-2-propyl sulfide (Table 5, entry 17): 500 μL of stock solution A and NaO*t*Bu (98 mg, 1.02 mmol) were used; column chromatography: hexane/ethyl acetate 20:1, then 5:1; colorless oil (93% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.50$ (d, $J=8.0$ Hz, 2H), 7.33 (d, $J=8.0$ Hz, 2H), 4.91 (q, $J=6.6$ Hz, 1H), 1.95 (brs, 1H), 1.50 (d, $J=6.6$ Hz, 3H), 1.28 (s, 9H); ^{13}C NMR ($CDCl_3$): $\delta=146.3$, 137.5 (2C), 131.5, 125.4 (2C), 70.0, 45.8, 30.9 (3C), 25.1; elemental analysis calcd (%) for $C_{12}H_{18}OS$: C 68.52, H 8.63; found: C 68.49, H 8.63.

4-(1-Hydroxyethyl)phenyl 2-methyl-2-propyl sulfide (Table 5, entry 18). 500 μL of stock solution A and Cs_2CO_3 (359 mg, 1.10 mmol) were used; 67% yield.

2-Fluorophenyl octyl sulfide (Table 5, entry 19): 100 μL of stock solution A were used; column chromatography; hexane/ethyl acetate 50:1 mixture (78% yield). It could not be separated of the corresponding aryl sulfide from the reaction at C–F bond (8% yield). The following spectroscopic data were obtained from the mixture. ^{1}H NMR ($CDCl_3$): $\delta=7.28$–7.24 (m, 1H), 7.11–7.06 (m, 1H), 7.00–6.92 (m, 2H), 2.80 (t, $J=7.3$ Hz, 2H), 1.53 (quint, $J=7.6$ Hz, 2H), 1.40–1.27 (m, 2H), 1.18 (brs, 8H), 0.79 (t, $J=6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=161.2$ (d, $^1J_{C,F}=244.6$ Hz), 131.4, 127.7 (d, $^3J_{C,F}=7.7$ Hz), 124.2 (d, $^3J_{C,F}=3.9$ Hz), 123.7 (d, $^2J_{C,F}=27.6$ Hz), 115.4 (d, $^2J_{C,F}=23.0$ Hz), 33.1, 31.7, 29.1 (2C), 29.0, 28.6, 22.5, 14.0.

2-Fluorophenyl 1-methylpropyl sulfide (Table 5, entry 20): 250 μL of stock solution A were used; column chromatography: hexane; colorless liquid (98% yield). Traces of the product of dithiolation were observed and could not be separated. ^{1}H NMR ($CDCl_3$): $\delta=7.42$ (td, $J=7.6$, 1.8 Hz, 1H), 7.26–7.21 (m, 1H), 7.09–7.03 (m, 2H), 3.22 (sext, $J=6.6$ Hz, 1H), 1.70–1.61 (m, 1H), 1.59–1.47 (m, 1H), 1.25 (d, $J=6.6$ Hz, 3H), 1.00 (t, $J=7.4$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=162.3$ (d, $^1J_{C,F}=245.4$ Hz), 134.7, 128.9 (d, $^3J_{C,F}=8.4$ Hz), 124.1 (d, $^3J_{C,F}=3.8$ Hz), 122.1 (d, $^2J_{C,F}=17.6$ Hz), 115.6 (d, $^2J_{C,F}=13.8$ Hz), 44.3, 29.5, 20.3, 11.2.

Benzyl 4-benzoylphenyl sulfide (Table 5, entry 21):[58] 10 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 20:1, then 5:1; white solid (93% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.75$ (d, $J=8.3$ Hz, 2H), 7.71 (d, $J=8.3$ Hz, 2H), 7.59–7.55 (m, 1H), 7.47 (t, $J=7.6$ Hz, 2H), 7.38 (d, $J=7.6$ Hz, 2H), 7.35–7.25 (m, 5H), 4.23 (s, 2H); ^{13}C NMR ($CDCl_3$): $\delta=195.6$, 143.4, 137.6, 136.2, 134.3, 132.1, 130.5 (2C), 129.7 (2C), 128.62 (2C), 128.55 (2C), 128.1 (2C), 127.4, 126.6 (2C), 37.1.

Benzyl 4-benzoylphenyl sulfide (Table 5, entry 22): No catalyzed reaction. NaO*t*Bu (106 mg, 1.10 mmol) were used; 86% yield.

4-Cyanophenyl cyclohexyl sulfide (Table 5, entry 23):[48] 10 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 20:1; white solid (90% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.53$ (d, $J=8.8$ Hz, 2H), 7.35 (d, $J=8.8$ Hz, 2H), 3.32 (tt, $J=10.2$, 3.5 Hz, 1H), 2.06–2.03 (m, 2H), 1.84–1.80 (m, 2H), 1.69–1.65 (m, 1H), 1.49–1.27 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta=143.9$, 132.1 (2C), 128.4 (2C), 118.8, 108.3, 44.8, 32.8 (2C), 25.8, 25.5 (2C).

4-Cyanophenyl cyclohexyl sulfide (Table 5, entry 24): No catalyzed reaction. NaO*t*Bu (106 mg, 1.10 mmol) were used and the reaction heated for 48 h; 79% yield, 91% conversion.

2-Cyanophenyl 2-methyl-2-propyl sulfide (Table 5, entry 25):[59] 250 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 50:1, then 20:1; yellow liquid (80% yields). ^{1}H NMR ($CDCl_3$): $\delta=7.73$ (dd, $J=7.6$, 1.5 Hz, 1H), 7.71–7.69 (m, 1H), 7.58 (td, $J=7.6$, 1.5 Hz, 1H), 7.49 (td, $J=7.5$, 1.2 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$): $\delta=138.7$, 136.4, 133.5, 132.1, 129.1, 121.1, 118.0, 48.7, 30.8 (3C).

2-Cyanophenyl 2-methyl-2-propyl sulfide (Table 5, entry 26): No catalyzed reaction. NaO*t*Bu (106 mg, 1.10 mmol) and the reaction heated for 24 h; 77% yield.

3-Cyanophenyl phenyl sulfide (Table 6, entry 1):[54] 100 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (93% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.46$–7.31 (m, 9H); ^{13}C NMR ($CDCl_3$): $\delta=139.8$, 133.2 (2C), 132.7, 132.0, 131.5, 129.7 (2C), 129.5, 129.4, 128.7, 118.1, 113.2.

3-Benzoylphenyl phenyl sulfide (Table 6, entry 2): 100 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 50:1, then 20:1; colorless oil (95% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.75$–7.71 (m, 3H), 7.62 (dt, $J=7.6$, 1.3 Hz, 1H), 7.57–7.53 (m, 1H), 7.48–7.23 (m, 9H); ^{13}C NMR ($CDCl_3$): $\delta=195.7$, 138.3, 137.2, 136.9, 134.1, 133.6, 132.5, 131.9 (2C), 131.2, 129.9 (2C), 129.3 (2C), 128.9, 128.2 (2C), 128.1, 127.7; elemental analysis calcd (%) for $C_{19}H_{14}OS$: C 78.59, H 4.86; found: C 78.65, H 4.87.

3-(4-Methoxyphenylsulfanyl)benzoic acid (Table 6, entry 3):[54] 250 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 3:1, then 1:1; white solid (74% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.90$ (brs, 1H), 7.86–7.83 (m, 1H), 7.45 (d, $J=9.0$ Hz, 2H), 7.36–7.31 (m, 2H), 6.92 (d, $J=9.0$ Hz, 2H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta=171.8$, 160.1, 140.1, 135.9 (2C), 132.6, 129.9, 129.0, 128.9, 127.2, 122.8, 115.2 (2C), 55.3.

3-Phenylsulfanylbenzamide (Table 6, entry 4):[60] 250 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 1:1; white solid (70% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.75$ (t, $J=1.8$ Hz, 1H), 7.65 (dt, $J=7.6$, 1.3 Hz, 1H), 7.43–7.26 (m, 7H), 6.40–6.18 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=168.9$, 137.4, 134.3, 134.2, 133.5, 131.8 (2C), 129.4 (2C), 129.3, 128.9, 127.7, 125.6.

Methyl 3-phenylsulfanylbenzoate (Table 6, entry 5):[41] 250 μL of stock solution C and KO*t*Bu (123 mg, 1.10 mmol) were used. The reaction was conducted in toluene (1.5 mL); column chromatography: hexane/ethyl acetate 50:1, then 20:1; colorless liquid (80% yield; 10–15% of *tert*-butyl ester derivative was also observed). ^{1}H NMR ($CDCl_3$): $\delta=8.01$ (t, $J=1.8$ Hz, 1H), 7.88 (dt, $J=7.9$, 1.3 Hz, 1H), 7.46 (m, 1H), 7.38–7.25 (m, 6H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta=166.4$, 137.0, 134.6, 134.5, 131.6 (2C), 131.3, 131.1 (2C), 129.3, 129.1, 127.9, 127.6, 52.2.

***N*-(3-Phenylsulfanyl)phenyl acetamide** (Table 6, entry 6): 250 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 1:1; colorless oil (99% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.80$ (brs, 1H), 7.46 (d, $J=8.1$ Hz, 1H), 7.39 (t, $J=1.8$ Hz, 1H), 7.36–7.19 (m, 6H), 7.02 (d, $J=7.8$ Hz, 1H), 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$): $\delta=168.7$, 138.6, 136.8, 134.9, 131.5 (2C), 129.5, 129.1 (2C), 127.3, 126.1, 121.4, 118.4, 24.4; elemental analysis calcd (%) for $C_{14}H_{13}NOS$: C 69.11, H 5.39, N 5.76; found: C 69.04, H 5.37, N 5.77.

3-Phenylsulfanylaniline (Table 6, entry 7):[61] 250 μL of stock solution A were used; column chromatography: hexane/ethyl acetate 5:1; yellow oil (91% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.35$–7.32 (m, 2H), 7.29–7.20 (m, 3H), 7.05 (t, $J=8.1$ Hz, 1H), 6.73–6.68 (m, 1H), 6.61–6.09 (m, 1H), 6.53–6.50 (m, 1H), 3.60 (brs, 2H); ^{13}C NMR ($CDCl_3$): $\delta=147.0$, 136.3, 135.6, 130.9 (2C), 129.8, 129.0 (2C), 126.8, 120.8, 116.9, 113.8.

4-(2-Isopropylphenylsulfanyl)phenol (Table 6, entry 8): A solution of $Pd(OAc)_2$ (4.4 mg) and CyPF-*t*Bu (11 mg) in DME (1 mL) was used as catalyst; column chromatography: hexane/ethyl acetate 20:1, then 5:1; pale yellow oil (91% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.22$–7.16 (m, 3H), 7.13–7.08 (m, 1H), 7.00–6.93 (m, 2H), 6.74–6.70 (m, 2H), 5.28 (brs, 1H), 3.43 (m, 1H), 1.16 (dd, $J=6.8$, 1.8 Hz, 6H); ^{13}C NMR ($CDCl_3$): $\delta=155.3$, 147.7, 135.5, 134.4 (2C), 130.1, 126.7, 126.3, 125.6, 125.5, 116.4 (2C), 30.2, 23.2 (2C); elemental analysis calcd (%) for $C_{15}H_{16}OS$: C 73.73, H 6.60; found: C 73.45, H 6.64.

2-Fluorophenyl phenyl sulfide (Table 6, entry 9):[62] 1000 μL of stock solution C and KO*t*Bu (123 mg, 1.10 mmol) were used. The reaction was conducted in toluene (1.5 mL); column chromatography: hexane was used as eluent; colorless liquid (96% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.18$–7.05 (m, 7H), 6.94–6.86 (m, 2H); ^{13}C NMR ($CDCl_3$): $\delta=161.0$ (d, $^1J_{C,F}=$

246.9 Hz), 134.0, 133.3, 130.8 (2C), 129.3, 129.2 (2C), 127.2, 124.6 (d, $^3J_{C,F}=10.7$ Hz), 122.6 (d, $^2J_{C,F}=17.6$ Hz), 115.8 (d, $^2J_{C,F}=22.23$ Hz).

2-Cyanophenyl phenyl sulfide (Table 6, entry 10):[59] 250 μL of stock solution A and NaO*t*Bu (106 mg, 1.10 mmol) were used; column chromatography: hexane/ethyl acetate 20:1 mixture; colorless liquid (99% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.54$ (d, $J=8.0$ Hz, 1H), 7.39–7.37 (m, 2H), 7.34–7.29 (m, 4H), 7.19–7.15 (m, 1H), 7.03 (d, $J=8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$): $\delta=142.1$, 133.5, 133.4 (2C), 132.9, 131.6, 129.7, 129.6 (2C), 128.8, 126.3, 116.8, 112.6.

2-Cyanophenyl phenyl sulfide (Table 6, entry 11): No catalyzed reaction. NaO*t*Bu (106 mg, 1.10 mmol) and the reaction heated for 24 h; 87% yield.

Synthesis of [(CyPF-*t*Bu)PdCl$_2$]: Josiphos CyPF-*t*Bu (55 mg, 0.10 mmol) was added to a solution of $(CH_3CN)_2PdCl_2$ (26 mg, 0.10 mmol) in CH_2Cl_2 (5.0 mL) and the resulting mixture was stirred for 30 min at room temperature. The reaction mixture was filtered through Celite and the resulting solution concentrated under vacuum to approximately 1.0 mL. Red needle crystals (65 mg, 90% yield) were obtained by layering with hexane and cooling at −10 °C. ^{1}H NMR ($CDCl_3$): $\delta=4.85$ (s, 1H), 4.55 (s, 1H), 4.53 (s, 1H), 4.25 (s, 5H), 3.60–3.75 (m, 1H), 3.00–3.10 (m, 1H), 2.50–2.60 (m, 1H), 2.27–2.90 (m, 1H), 2.13–2.25 (m, 2H), 2.00–2.10 (m, 1H), 1.97 (dd, $J=9.0$, 7.5 Hz, 3H), 1.70–1.95 (m, 4H), 1.20–1.30 (m, 8H), 1.63 (d, $J=13.0$ Hz, 9H), 1.30–1.45 (m, 4H), 1.23 (d, $J=14.5$ Hz, 9H); ^{13}C NMR ($CDCl_3$): $\delta=96.5$ (dd, $J=13.3$, 5.5 Hz), 71.9 (d, $J=2.5$ Hz), 69.9 (d, $J=9.1$ Hz), 69.8 (5C), 69.6 (d, $J=9.2$ Hz), 69.3 (t, $J=5.7$ Hz), 41.60 (d, $J=35.5$ Hz), 41.57 (d, $J=8.2$ Hz), 40.6 (d, $J=11.2$ Hz), 37.6 (d, $J=35.5$ Hz), 34.5 (t, $J=9.1$ Hz), 32.0 (d, $J=1.9$ Hz, 3C), 31.1 (d, $J=1.9$ Hz, 3C), 30.0, 29.2, 28.1, 27.6 (d, $J=6.8$ Hz), 27.3 (d, $J=10.2$ Hz), 27.0 (d, $J=12.6$ Hz), 26.9 (d, $J=5.2$ Hz), 26.8 (d, $J=3.8$ Hz), 26.1 (d, $J=1.9$ Hz), 25.6, 18.0 (d, $J=6.7$ Hz); elemental analysis calcd (%) for $C_{32}H_{52}Cl_2FeP_2Pd$: C 52.51, H 7.16; found: C 52.72, H 7.38.

Preparation of stock solution D (1.0×10^{-2} M): [(CyPF-*t*Bu)PdCl$_2$] (7.3 mg) was diluted in THF (1.0 mL) and the resulting orange solution was stirred at room temperature for 1 min prior to subsequent reactions.

General procedure for the palladium-catalyzed coupling of aryl chlorides with thiols using [(CyPF-*t*Bu)PdCl$_2$] complex: The appropriate quantity of stock solution D was added to a 4 mL vial containing the aryl chloride (1.00 mmol) and base (1.10 mmol) in 1.5 mL of solvent (NaO*t*Bu and DME for aliphatic thiols, KO*t*Bu and toluene for aromatic thiols, unless otherwise stated). The thiol (1.00 mmol) was then added, and the vial sealed with a cap containing a PTFE septum. The mixture was heated at 110 °C until the chloroarene was consumed, as determined by GC. Silica gel (0.5 g) was added and the solvents were evaporated under reduced pressure. The crude residue was purified by column chromatography on silica gel using hexane or a mixture of hexane and ethyl acetate as eluent. Aryl sulfides were isolated in the yields reported in Table 7.

4-Methoxyphenyl octyl sulfide (Table 7, entry 1): 100 μL of stock solution D were used; 97% yield.

Octyl phenyl sulfide (Table 7, entry 2): 50 μL of stock solution D were used; 97% yield.

Cyclohexyl 4-methylphenyl sulfide (Table 7, entry 3): 50 μL of stock solution D were used; 94% yield.

2-Methylbutyl 3-methoxyphenyl sulfide (Table 7, entry 4): 50 μL of stock solution D were used; column chromatography: hexane/ethyl acetate 50:1; colorless liquid (98% yield). ^{1}H NMR ($CDCl_3$): $\delta=7.07$ (t, $J=7.9$ Hz, 1H), 6.80–6.76 (m, 2H), 6.59–6.56 (m, 1H), 3.67 (s, 3H), 2.84 (dd, $J=12.5$, 5.9 Hz, 1H), 2.64 (dd, $J=12.5$, 7.6 Hz, 1H), 1.60–1.52 (m, 1H), 1.49–1.39 (m, 1H), 1.22–1.11 (m, 1H), 0.91 (d, $J=6.6$ Hz, 3H), 0.81 (t, $J=7.1$ Hz, 3H); ^{13}C NMR ($CDCl_3$): $\delta=159.6$, 138.8, 129.4, 120.5, 113.7, 110.9, 55.0, 40.2, 34.3, 28.7, 18.8, 11.1; elemental analysis calcd (%) for $C_{12}H_{18}OS$: C 68.52, H 8.63; found: C 68.32, H 8.68.

Octyl 2-thiophenyl sulfide (Table 7, entry 5). 50 μL of stock solution D were used; 93% yield.

2,5-Dimethylphenyl 2-methyl-2-propyl sulfide (Table 7, entry 6): 3.7 mg of [(CyPF-*t*Bu)PdCl$_2$] were used; 96% yield.

4-Methylphenyl 4-methoxyphenyl sulfide (Table 7, entry 7): 250 μL of stock solution D were used; 88% yield.

4-Methylphenyl phenyl sulfide (Table 7, entry 8): 250 μL of stock solution D and LiHMDS (184 mg, 1.10 mmol) were used; 97% yield.

Phenyl 4-trifluoromethylphenyl sulfide (Table 7, entry 9): 3.7 mg of [(CyPF-*t*Bu)PdCl$_2$] were used; 90% yield.

2-Isopropylphenyl 4-methoxyphenyl sulfide (Table 7, entry 10): 250 μL of stock solution D were used; 94% yield.

1-Naphthalenyl phenyl sulfide (Table 7, entry 11): 100 μL of stock solution D were used; 98% yield, <2% of symmetrical sulfides were detected.

2-Methylphenyl phenyl sulfide (Table 7, entry 12): 3.7 mg of [(CyPF-*t*Bu)PdCl$_2$] were used; 77% yield, 18% of symmetrical sulfides were also formed.

3-Cyanophenyl 2-methyl-2-propyl sulfide (Table 7, entry 13): 50 μL of stock solution D were used; 91% yield.

3-Benzoylphenyl cyclohexyl sulfide (Table 7, entry 14): 100 μL of stock solution D were used; 80% yield.

3-Phenylsulfanylbenzamide (Table 7, entry 15): 3.7 mg of [(CyPF-*t*Bu)PdCl$_2$] and NaO*t*Bu (230 mg, 2.40 mmol) were used; 66% yield.

3-Phenylsulfanylaniline (Table 7, entry 16): 3.7 mg of [(CyPF-*t*Bu)PdCl$_2$] and NaO*t*Bu (230 mg, 2.40 mmol) were used; 92% yield.

3-(2-Methylbutylsulfanyl)phenol (Table 7, entry 17): 3.7 mg of [(CyPF-*t*Bu)PdCl$_2$] and NaO*t*Bu (230 mg, 2.40 mmol) were used; 96% yield.

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