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Thioether-Promoted Direct Olefination of Polyfluoroarenes Catalyzed by Palladium

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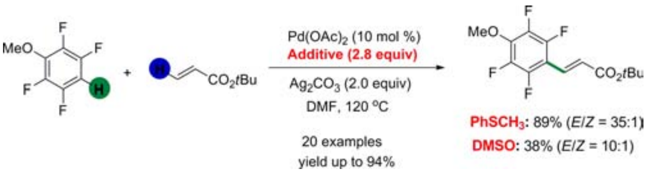
ABSTRACT



A methyl(phenyl)sulfane-promoted direct olefination of polyfluoroarenes catalyzed by palladium has been reported. With use of this new thioether ligand, a high reaction efficiency and excellent *E*/*Z* ratio of desired olefinated polyfluoroarenes were obtained. This represents a first example of thioether promoted oxidative Heck reaction.

Polyfluoroaryl groups are an important structural motif found in a wide range of bioactive compounds and functional materials.[1] In particular, such fluorinated compounds constitute a distinct class of active materials in liquid crystals and electronic devices.[2] Over the past few years, many efforts have been made to access polyfluoroaryl-substituted compounds, and some impressive methods of transition-metal-catalyzed direct functionalization of polyfluoroarenes have been developed.[3,4] Since the use of simple and readily available polyfluoroarenes as starting material without requirement of a "prefunctionalization"

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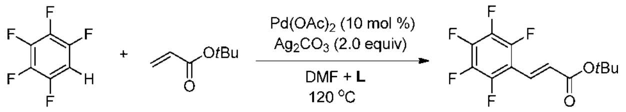
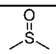
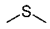
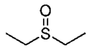
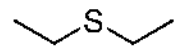
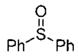
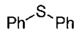
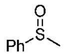
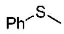
process, this direct C−H bond functionalization strategy represents an attractive and ideal alternative to the traditional techniques.[5,6] Very recently, we reported a first example of Pd-catalyzed direct olefination of polyfluoroarenes,[4a] which represents one of the rare examples of catalytic direct olefination of electron-deficient arenes.[7] During the studies, it was found that DMSO plays an important role for the reaction efficiency and may functionalize as a ligand to active the palladium catalyst.[8] This finding inspired us to question that whether other DMSO derivatives or sulfur containing compounds, such as thioethers, could also benefit the reaction efficiency, and improve the yields of some "inert" substrates, such as 3-substituted tetrafluorobenzene, previously affording low yields. Herein, we report a methyl(phenyl)sulfane-promoted direct olefination of polyfluoroarenes catalyzed by palladium. With use of this new thioether ligand, high yields of desired olefinated polyfluoroarenes were obtained. In particular, for 3-substituted tetrafluorobenezenes, much higher yields than our previous results were afforded. This represents the first example of thioether promoted oxidative Heck reaction.

Initially, different sulfoxides were tested by treatment of pentafluorobenzene **1** (1.0 equiv) with *tert*-butyl acrylate (2.0 equiv) and Ag_2CO_3 (2.0 equiv) in the presence of $Pd(OAc)_2$ (10 mol %) and sulfoxide (2.8 equiv) in DMF at 120 °C (Table 1). It turned out that diethyl sulfoxide is better than DMSO, providing **3a** in a slightly higher yield (Table 1, entry 2), while diphenyl sulfoxide and methyl (phenyl) sulfoxide showed little or no effect (Table 1, entries 3 and 4). On the basis of these results, a series of sulfanes corresponding to the above sulfoxides were further examined to compare the activities between these two types of similar ligands (Table 1, entries 5−8). In sharp contrast to sulfoxides, a reverse activity was observed for sulfanes. Dimethylsulfane and diethylsulfane almost inhibited the reaction (Table 1, entries 5 and 6), but with increasing the size of substituents on the sulfanes, higher yields of **3a** were obtained (Table 1, entries 7−8), in which methyl(phenyl)sulfane is superior to diphenylsulfane, providing the highest yield (80%) (Table 1, entry 8). However, only 30% yield of **3a** was provided when methyl (phenyl) sulfoxide was employed (Table 1, entry 4). These results demonstrated that PhSMe may functionalize as a ligand to activate palladium species and benefit the reaction efficiency.[9] Additionally, a GC−MS analysis of the reaction showed only PhSMe was observed, and no formation of methyl (phenyl) sulfoxide generated from the oxidation of PhSMe was detected during the reaction, thus further confirming that PhSMe itself has a beneficial effect on the reaction. This is opposite to our common knowledge, as thioethers usually poison the palladium catalyst and inhibit the reaction.[10] We reasoned that the highest activity of PhSMe might be ascribed to the proper coordination ability of PhSMe to palladium,[11] leading to an active palladium intermediate. However, the detailed mechanism remains a point of discussion.

Table 1. Ligand Effect of Pd-Catalyzed Direct Olefination of Pentafluorobenzene **1** with *tert*-Butyl Acrylate **2a**[a]



1a **2a** **3a**

entry	L	yield (%) (E/Z)[b]	entry	L	yield (%) (E/Z)[b]
1		73 (17:1)	5		7[c]
2		76 (16:1)	6		5[c]
3		8[c]	7		50 (15:1)
4		30 (16:1)	8		80 (20:1)

[a] Reaction conditions (unless otherwise specified): **1a** (0.6 mmol), **2a** (2.0 equiv), $Pd(OAc)_2$ (10 mol %), **L** (2.8 equiv, **L**/$Pd(OAc)_2$ = 28:1, mol/mol), and DMF (2.4 mL) at 120 °C for 12 h. [b] Isolated yield and the number in parentheses is the *E*/*Z* ratio of **3a** determined by ^{19}F NMR. [c] NMR yield determined by ^{19}F NMR using fluorobenzene as internal standard.

With the identification of the optimal ligand PhSMe, the substrate scope with respect to direct olefination of pentafluorobenzene was illustrated in Scheme 1. Both electron-deficient and electron-rich alkenes provided alkenylated pentafluorobenzenes in good yields. Importantly, higher yields and stereoselectivities (*E*/*Z*) than our previous results were obtained for electron-deficient alkenes (**3a**−**d**). For aromatic alkenes (**3e**−**g**), a substrate bearing an electron-donating group was more reactive than that of electron-withdrawing one, providing an excellent yield (94%). However, in the cases of **3d** and **3e**, slightly lower yields were obtained. Notably, protected allylamine also underwent reaction smoothly, with **3h** obtained as the major product, thus providing a good opportunity for further transformation. The X-ray crystallographic analysis of **3h** further confirmed its structure (see the Supporting Information). In addition, more electron-rich alkene, such as enamide, also furnished its corresponding product in good yield with high stereoselectivity (**3i**). However, the enol ether

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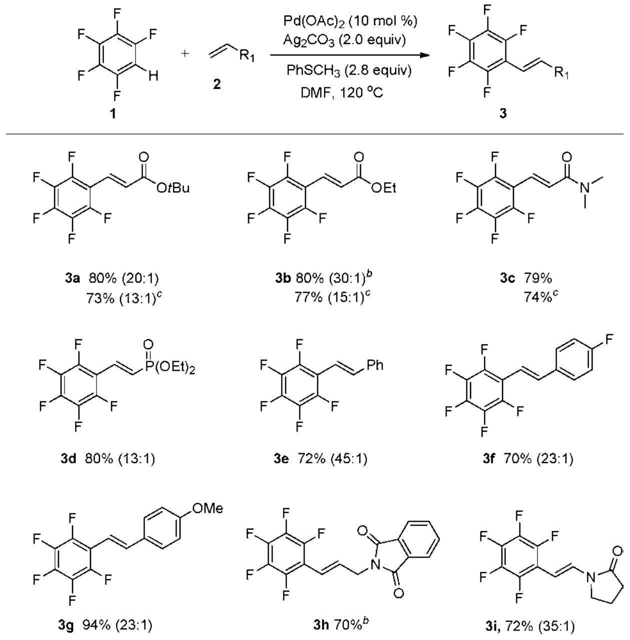
1-(vinyloxy)butane provided a mixture of olefinated products in 42% yield (determined by ^{19}F NMR). Cyclohexene was a unsuitable substrate, leading to a poor yield (10% determined by ^{19}F NMR).

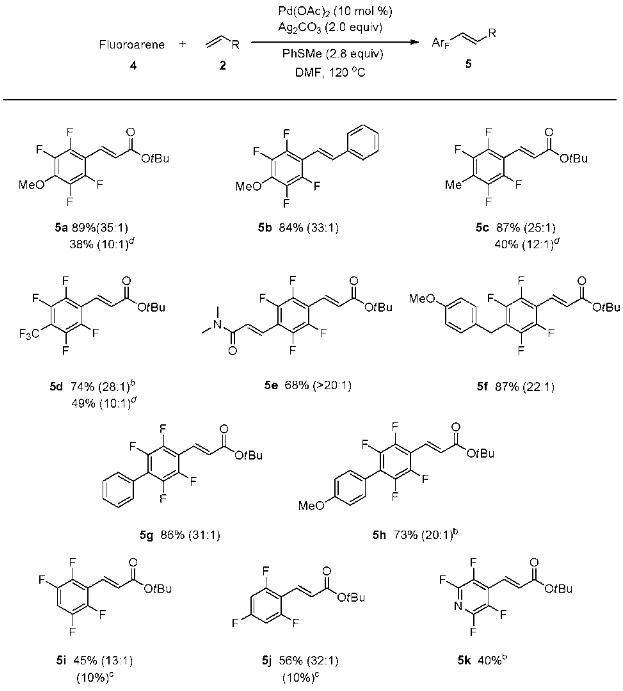
Scheme 1. Pd-Catalyzed Direct Olefination of Pentafluorobenzene **1** with Various Alkenes **2**[a]



[a] Reaction conditions (unless otherwise specified): **1** (0.6 mmol), **2** (2.0 equiv), Pd(OAc)$_2$ (10 mol %), PhSCH$_3$ (2.8 equiv), DMF (2.4 mL), 120 °C, 9 h. Number in parentheses is the ratio of *E*/*Z*. [b] 1.0 equiv of **1** was used. [c] Previous method (ref 4a): **1** (0.6 mmol), **2** (2.0 equiv), Pd(OAc)$_2$ (10 mol %), DMSO (2.8 equiv), DMF (2.4 mL), 120 °C, 9 h.

In addition to the demonstrated broad range of polyfluoroarenes, various fluoroarenes **4** containing three or four fluorines were also competent partners (Scheme 2). It is noteworthy that the "inert" substrates, such as 3-substituted tetrafluorobenzenes that previously furnished their corresponding products in low yields, afforded alkenylated products in high yields and excellent stereoselectivities with using only 1.0 equiv of alkenes (**5a**–**h**), thus featuring the power of the thioether ligand PhSMe. For example, a much higher yield of **5a** than previously was obtained when PhSMe was used as a ligand (**5a**). Similar significant results were also observed when 1,2,4,5-tetrafluoro-3-methylbenzene and 1,2,4,5-tetrafluoro-3-trifluoromethylbenzene were used as substrates (**5c**–**d**). Additionally, other substituents on the tetrafluorobenzene at the para position to the hydride, such as alkenyl, benzyl and aryl groups, also proceeded smoothly (**5e**–**f**), thus allowing the facile synthesis of highly functionalized polyfluoroarene derivatives. For the substrate bearing more than one reaction site, moderate yields of mono-alkyenylated products still could be obtained (**5i**–**j**). A pyridyl group was also compatible with the coupling reaction, providing a lower yield than previous result (**5k**).

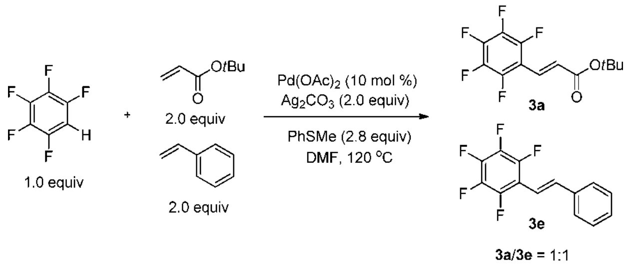
Scheme 2. Pd-Catalyzed Direct Olefination of Fluoroarenes **4** with Various Alkenes **2**[a]



[a] Reaction conditions (unless otherwise specified): **4** (0.6 mmol), **2** (1.0 equiv), DMF (2.4 mL) for 9 h. Number in parentheses is the ratio of *E*/*Z*. [b] 2.0 equiv of **2** was used. [c] 3.0 equiv of **1** was used, and 10% of dialkenylated product was obtained. [d] Previous method (ref 4a): **1** (0.6 mmol), **2** (2.0 equiv), Pd(OAc)$_2$ (10 mol %), DMSO (2.8 equiv), DMF (2.4 mL), 120 °C, 9 h.

A competitive reaction between electron-deficient and electron-rich alkenes with pentafluorobenzene was also conducted (Scheme 3), providing their corresponding products **3a** and **3e** in an almost 1:1 ratio (determined by ^{19}F NMR), thus demonstrating that the direct olefination of polyfluoroarenes has no bias on the nature of alkenes under the present reaction conditions.

Scheme 3. Competitive Reaction



In summary, a thioether-promoted direct olefination of polyfluoroarenes catalyzed by palladium has been developed. The power of the new ligand PhSMe has been demonstrated by the reaction of those previous 'inert' substrates to provide high yields, thus offering us a new choice to discover more efficient catalytic systems. Further investigation of the reaction mechanism and using thioether as a ligand for other reactions are now in progress.

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Supporting Information Available. Detailed experimental procedures and characterization data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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The authors declare no competing financial interest.