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A General Method for Palladium-Catalyzed Reactions of Primary Sulfonamides with Aryl Nonaflates

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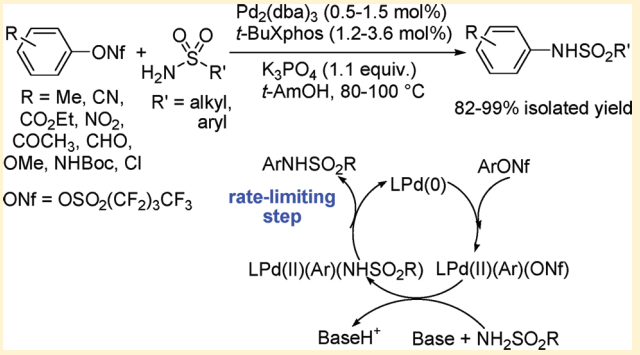
Supporting Information

ABSTRACT: A general method for Pd-catalyzed sulfonamidation of aryl nonafluorobutanesulfonates (aryl nonaflates) is described. A biaryl phosphine ligand, *t*-BuXPhos, formed the most active catalyst, and K_3PO_4 in *tert*-amyl alcohol was found to be the optimal base−solvent combination for the reaction. The reaction conditions were tolerant of various functional groups such as cyano, nitro, ester, aldehyde, ketone, chloride, carbamate, and phenol. Heterocyclic aryl nonaflates were found to be suitable coupling partners. High yields of the coupled products were obtained from the reactions between inherently disfavored substrates such as electron-rich nonaflates and electron-poor sulfonamides. Kinetic data suggest reductive elimination to be the rate-limiting step for the reaction. The only limitation of this methodology that we have identified is the inability of 2,6-disubstituted aryl nonaflates to efficiently participate in the reaction.



INTRODUCTION

N-Aryl sulfonamides are common functional groups in molecules of medicinal interest.[1] One of the most common approaches to secondary sulfonamide synthesis is the reaction of aromatic amines with sulfonic acid derivatives. However, this route requires prior preparation of the amine. In many cases compounds containing aromatic amines are genotoxic and are undesirable as intermediates in the synthesis of active pharmaceutical ingredients (API).[2] An alternate route to *N*-aryl sulfonamides is the metal-catalyzed coupling of aryl halides or pseudohalides with primary sulfonamides. Such an approach would facilitate SAR studies if it could be applicable to a wide range of target molecules as well as be advantageous on large scale, because it would avoid potential genotoxic intermediates.

The substrate scope of Pd-catalyzed reactions of primary sulfonamides with aryl pseudohalides has not been explored in detail. Intermolecular Pd-catalyzed reactions of aryl halides with primary sulfonamides have been reported,[3−10] but only a few isolated examples of couplings of aryl pseudohalides with sulfonamides are known.[11−15] Prompted by the need to convert structurally diverse aryl alcohols to a variety of secondary sulfonamides, we initiated an investigation to identify a practical and general method for the coupling of aryl pseudohalides with electronically and sterically diverse primary sulfonamides. This methodology has significant synthetic value because of the diversity of commercially available phenols, the ubiquity of phenols as synthetic intermediates, and the demonstrated utility of aryl pseudohalides in several other Pd-catalyzed cross-coupling reactions.

One of the challenges associated with Pd-catalyzed couplings of sulfonamides is the need for harsher reaction conditions compared to reactions of other nitrogen-based nucleophiles such as amides, carbamates, and ureas, most likely due to the lower nucleophilicity of sulfonamides.[3,4] Aryl triflates, the most commonly employed aryl pseudohalides, can undergo competitive hydrolysis under the reaction conditions required to effect sulfonamide coupling. Aryl nonafluorobutanesulfonates (aryl nonaflates, ArONf) on the other hand are significantly more resistant to nucleophilic cleavage and yet have reactivities similar to those of aryl triflates in Pd-catalyzed cross-coupling reactions.[16,17]

Herein, we report a general, efficient method for coupling aryl nonaflates with a variety of primary sulfonamides catalyzed by Pd complexes of readily available phosphine ligands.[18] Secondary sulfonamides were obtained in excellent yields and minimal (<1%) hydrolysis of the electrophile was observed under the reaction conditions.

RESULTS AND DISCUSSIONS

p-Methylbenzene nonaflate (**1a**) and methanesulfonamide (**2a**) were chosen as coupling partners during the initial identification of effective reaction conditions. A combination of $Pd_2(dba)_3$ and Xantphos (**I**) had been reported to form an active catalyst for the reaction of an enol triflate with *p*-toluenesulfonamide;[11] however, less than 1% product **3a** was observed using similar reaction conditions (Table 1, entry 1). The use of *t*-BuXantphos (**II**) as ligand also did not form **3a** in

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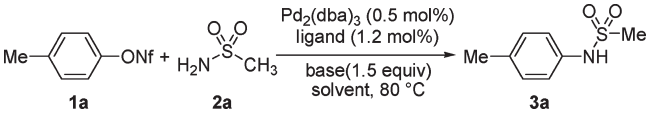
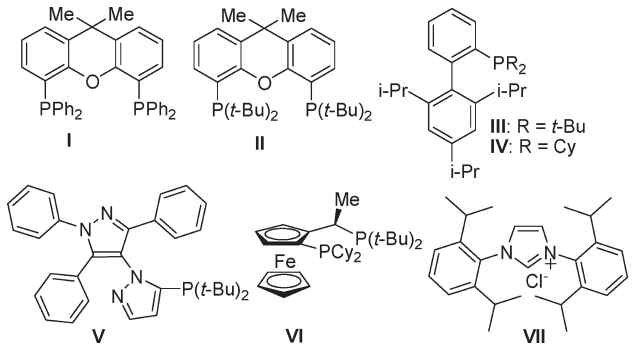
Table 1. Evaluation of Reaction Parameters for Pd-Catalyzed Sulfonamidation[a]



1a 2a 3a

entry	ligand	solvent	base	3a (%)[b]
1	**I**	1,4-dioxane	Cs_2CO_3	<1
2	**II**	1,4-dioxane	Cs_2CO_3	<1
3	**III**	1,4-dioxane	Cs_2CO_3	92
4	**III**	1,4-dioxane	K_3PO_4	94
5	**III**	*t*-AmOH	Cs_2CO_3	34
6	**III**	*t*-AmOH	K_3PO_4	93
7	**III**	*t*-AmOH	K_2CO_3	95
8	**IV**	*t*-AmOH	K_3PO_4	<1
9	**V**	*t*-AmOH	K_3PO_4	7
10	**VI**	*t*-AmOH	K_3PO_4	<1
11	**VII**	*t*-AmOH	K_3PO_4	<1

[a] All experiments were conducted with **1a** (0.78 mmol), **2a** (0.92 mmol), and base (1.15 mmol) in solvent (2.5 mL). [b] Assay yield based on HPLC analysis at 210 nm.

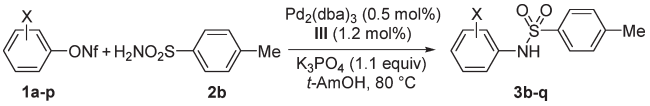


any appreciable amount (entry 2). On the other hand, Pd-complexes of *t*-BuXPhos (**III**) were successful in catalyzing the reaction, and **3a** was obtained in a high yield (>90%). In 1,4-dioxane, **3a** was obtained in similar yields using either Cs_2CO_3 or K_3PO_4 as the base (entries 3 and 4). In *tert*-amyl alcohol (2-methyl-2-butanol, *t*-AmOH) reactions employing Cs_2CO_3 were complicated by the production of significant amounts of the hydrolysis product, *p*-cresol (entry 5). However, K_3PO_4 and K_2CO_3 both afforded high yields of coupled product (entries 6 and 7), though K_3PO_4 provided slightly faster reaction rates.[19] Although *t*-AmOH and 1,4-dioxane provided essentially identical yields of the desired secondary sulfonamide, we preferred to use *t*-AmOH because of the known toxicity of 1,4-dioxane.

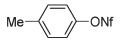
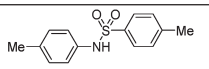
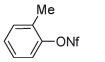
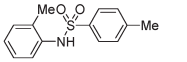
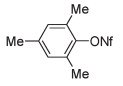
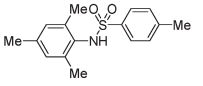
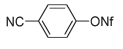
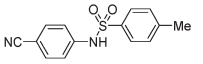
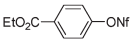
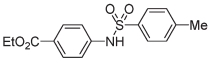
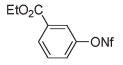
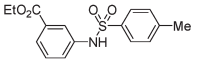
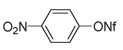
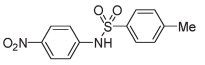
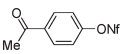
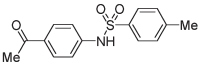
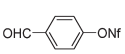
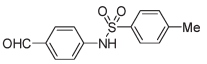
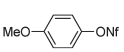
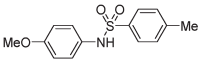
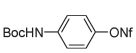
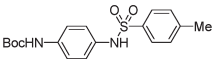
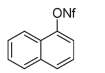
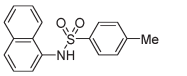
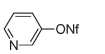
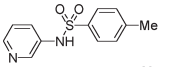
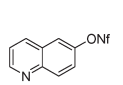
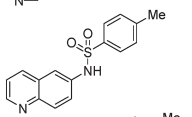
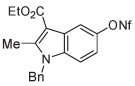
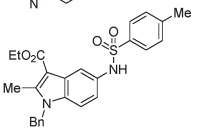
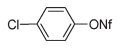
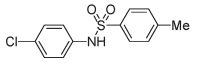
The presence of *tert*-butyl groups on the biaryl phosphine appears to be crucial to the success of the reaction as XPhos (**IV**) did not form **3a** in any appreciable amount (entry 8). Other ligands examined were less effective; Bipyphos (**V**) afforded **3a** in low yield (entry 9), and no product formation was observed in the presence of a bidentate phosphine or carbene ligand (entries 10 and 11).[14]

Having identified suitable conditions for the Pd-catalyzed sulfonamidation reaction, we next explored the generality of coupling

Table 2. Pd-Catalyzed Coupling of *p*-Toluenesulfonamide with Aryl Nonaflates



1a-p 2b 3b-q

Entry	Nonaflate		Product		Yield(%)[a]
1		**1a**		**3b**	89
2		**1b**		**3c**	96
3		**1c**		**3d**	20[b]
4		**1d**		**3e**	89
5		**1e**		**3f**	92
6		**1f**		**3g**	86
7[c]		**1g**		**3h**	92
8[d]		**1h**		**3i**	86
9[d]		**1i**		**3j**	82
10[e]		**1j**		**3k**	91
11		**1k**		**3l**	92
12		**1l**		**3m**	95
13[f]		**1m**		**3n**	80
14		**1n**		**3o**	86
15[f]		**1o**		**3p**	88
16[d]		**1p**		**3q**	86

[a] Isolated yield. Unless noted otherwise, all experiments were performed with aryl nonaflate (1 equiv), **2b** (1.2 equiv), K_3PO_4 (1.1 equiv), $Pd_2(dba)_3$ (0.005 equiv), and **III** (0.012 equiv) in *t*-AmOH (0.29 M) at 80 °C. [b] $Pd_2(dba)_3$ (0.025 equiv), **III** (0.06 equiv) at 120 °C. Approximate yield based on HPLC analysis. [c] $Pd_2(dba)_3$ (0.0025 equiv), **III** (0.006 equiv) for 1 h. [d] Aryl nonaflate (1.1 equiv) and **2b** (1.0 equiv). [e] $Pd_2(dba)_3$ (0.0075 equiv), **III** (0.018 equiv) at 90 °C. [f] $Pd_2(dba)_3$ (0.01 equiv), **III** (0.024 equiv), and Cs_2CO_3 (1.1 equiv) at 90 °C.

reactions of *p*-toluenesulfonamide (**2b**) with a variety of aryl nonaflates (Table 2). A high yield of the coupled product **3b** was obtained for the reaction of **1a** in the presence of 1 mol % Pd (entry 1). No effect on the efficiency of the reaction was observed

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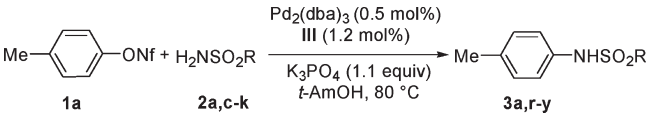
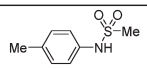
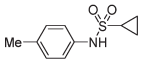
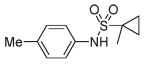
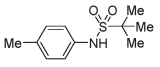
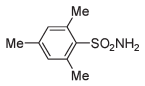
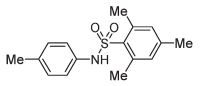
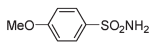
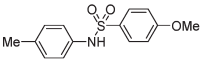
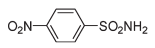
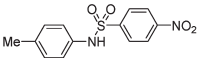
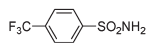
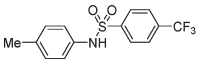
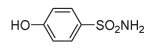
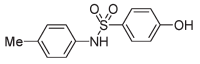
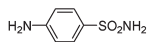
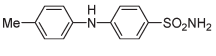
Table 3. Pd-Catalyzed Coupling of *p*-Methylbenzene Nonaflate with Sulfonamides



Entry	Sulfonamide		Product		Yield (%)[a]
1		**2a**		**3a**	94
2		**2c**		**3r**	99
3		**2d**		**3s**	91
4[b]		**2e**		**3t**	86
5		**2f**		**3u**	84
6		**2g**		**3v**	94
7[c]		**2h**		**3w**	82
8[c]		**2i**		**3x**	92
9		**2j**		**3y**	83
10		**2k**		**4**	82

[a] Isolated yield. Unless noted otherwise, all experiments were performed with **1a** (1 equiv), sulfonamide (1.2 equiv), K_3PO_4 (1.1 equiv), $Pd_2(dba)_3$ (0.005 equiv), and **III** (0.012 equiv) in *t*-AmOH (0.29 M) at 80 °C. [b] $Pd_2(dba)_3$ (0.01 equiv), **III** (0.024 equiv) at 100 °C. [c] $Pd_2(dba)_3$ (0.015 equiv), **III** (0.036 equiv), and Cs_2CO_3 (1.1 equiv) at 100 °C.

when sterically hindered *o*-methylbenzene nonaflate (**1b**) was used as an electrophile (entry 2). However, a further increase in the steric bulk on the aryl nonaflate was accompanied by a dramatic reduction in the efficiency of the reaction. The coupled product from reaction of mesityl nonaflate (**1c**) was observed in less than 20% yield even when the reaction was conducted at 120 °C with 5 mol % Pd (entry 3).[20]

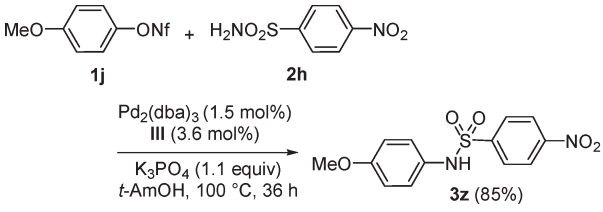
Although both electron-poor and electron-rich nonaflates generated the coupled products in high yields (entries 4−11), the reaction rate was highly dependent on the electron-donating ability of the substituent. For example, the reaction of *p*-nitrobenzene nonaflate (**1g**) proceeded to full conversion in less than 1 h at 80 °C in the presence of only 0.5 mol % Pd (entry 7),[21] while a higher catalyst loading (1.5 mol % Pd) and temperature (90 °C) were required to drive the reaction of *p*-methoxybenzene nonaflate (**1j**) to greater than 99% conversion after ∼16 h (entry 10).

The methodology was tolerant of base-sensitive functional groups such as nitrile, nitro, esters, ketones, and aromatic aldehydes (entries 4−9). Transesterification products that could arise from the reaction of solvent, *t*-AmOH, with ethyl ester were not detected in any significant amount under the reaction conditions (entries 5, 6, and 15). No competitive ketone arylation product was observed from an acetyl-substituted nonaflate (entry 8).[22] The reactions of heterocyclic aryl nonaflates such as pyridyl-3-nonaflate (**1m**) and quinolinyl-6-nonaflate (**1n**) also furnished the corresponding sulfonamides in high yields (entries 13 and 14). When *p*-chlorobenzene nonaflate (**1p**) was used as an electrophile (entry 16), insertion into the nonaflate to give **3q** was favored, although the product of coupling at both nonaflate and chloride was observed with an excess of sulfonamide. By running the reaction with a slight excess of nonaflate (1.1 equiv), a good yield of **3q** was realized, with only minor amounts of bis-coupled product (<3%).

Next, the generality of the coupling reaction of aryl nonaflate **1a** with a variety of sulfonamides was probed (Table 3). The reactions of several alkyl sulfonamides, ranging in steric bulk from methanesulfonamide to *tert*-butylsulfonamide, afforded the corresponding products in excellent yields (Table 3, entries 1−4). Although the reaction of methylcyclopropylsulfonamide (**2d**) proceeded to full conversion under standard conditions (80 °C with 1 mol % Pd), the reaction of *tert*-butylsulfonamide (**2e**) required a higher temperature (100 °C) and 2 mol % Pd to proceed to full conversion within 16 h. It is worth noting that sulfonamides similar to **3t** would be difficult to prepare by the traditional method of condensing an aromatic amine with a sulfonyl chloride because of the poor reactivity and general instability of *tert*-alkyl sulfonyl chlorides.[23,24]

A wide range of aromatic sulfonamides were found to be competent nucleophiles in this reaction. A sterically hindered aromatic sulfonamide, 2,4,6-trimethylbenzenesulfonamide (**2f**), was found to be a suitable substrate (entry 5). The reaction of an electron-rich aromatic sulfonamide, *p*-methoxybenzenesulfonamide (**2g**), afforded the corresponding product in high yield (entry 6). Remarkably, high yields of the coupled products were also obtained from the reactions of electron-poor sulfonamides (entries 7 and 8), albeit at higher temperature (100 °C) and catalyst loading (3 mol % Pd). When *p*-hydroxybenzenesulfonamide (**2j**) was used as the nucleophile, coupling at the sulfonamide was preferred over coupling at the phenol (entry 9). Arylation of sulfanilamide (**2k**) with **1a** preferentially occurred at the aniline (entry 10).

Finally, even the challenging substrate combination of an electron-rich nonaflate (**1j**) and an electron-poor sulfonamide (**2h**) was accomplished in excellent yield under slightly forcing conditions (3 mol % Pd, 100 °C, eq 1).



(1)

The reactivity of alkenyl nonaflates was also evaluated. These substrates were also competent electrophiles, but these reactions appeared to be more sensitive to adventitious water. A significant amount of β-tetralone was observed in the reaction of alkenyl nonaflate **5** with **2b** using the conditions developed for aryl nonaflates. Addition of 4 Å molecular sieves completely suppressed the hydrolysis of **5**, affording the coupled product **6** in acceptable yield (81%) (Scheme 1). The formation of 4-phenylcyclohexanone (∼10%) was observed in the reaction of alkenyl nonaflate **7** despite the addition of molecular sieves. The coupled product **8** was observed in approximately 60% yield by HPLC and LCMS analysis

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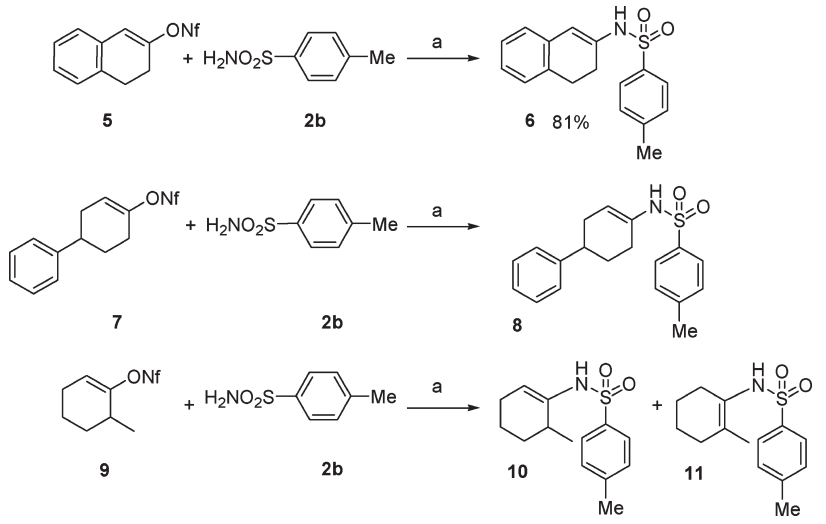
Scheme 1. Pd-Catalyzed Coupling of Alkenyl Nonaflates[a]



[a] Reagents and conditions: vinyl nonaflate (1 equiv), **2b** (1.2 equiv), K_3PO_4 (1.1 equiv), $Pd_2(dba)_3$ (0.005 equiv), **III** (0.012 equiv), and 4 Å molecular sieves (powdered) (200 wt %) in *t*-AmOH (0.29 M) at 80 °C.

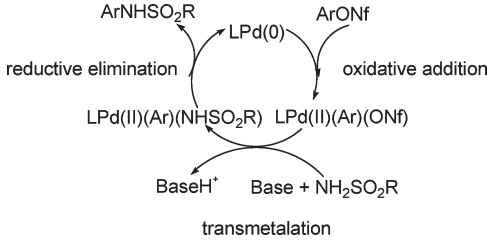


Figure 1. Proposed mechanism of the Pd-catalyzed sulfonamidation of aryl nonaflates.

of the reaction mixture but was isolated in only 10% yield and approximately 80% purity after column chromatography. This alkenyl sulfonamide appears to decompose to 4-phenylcyclohexanone and *p*-toluenesulfonamide on either a silica gel or an alumina column, and we were unable to purify the product to homogeneity. Surprisingly, the tertiary sulfonamide arising from further reaction of **8** with nonaflate **7** was also observed during the reaction in approximately 10% yield (HPLC). This is the only instance in which we have observed further reaction of any of the initially formed sulfonamide products. The formation of this byproduct could not be suppressed by performing the reaction in the presence of excess **2b** (3 equiv) or performing the reaction at a lower temperature (60 °C).

Alkenyl nonaflate **9** coupled with **2b** under the standard reaction conditions without observable hydrolysis to 2-methylcyclohexanone or formation of any tertiary sulfonamide product. However, in addition to the expected product **10**, a product arising from isomerization of the double bond (**11**) was also observed in the ^{1}H NMR spectra of the unpurified reaction mixture. As observed for **8**, the coupled products **10** and **11** also decomposed on silica gel column, and we were unable to isolate analytically pure product. Thus, the utility of this methodology for the preparation of alkenyl sulfonamides appears to be limited by the poor stability of the products to hydrolysis. In the case of stable alkenyl sulfonamides (e.g., **6**) the reaction may be preparatively useful.

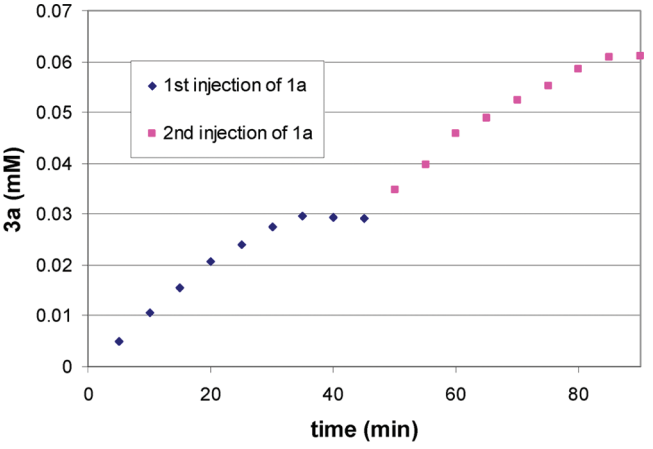


Figure 2. Plot of concentration of **3a** versus time. First injection of **1a**: the reaction was performed with **1a** (0.128 mmol) and **2a** (1.54 mmol), and the formation of **3a** was followed for 45 min by HPLC. Second injection of **1a**: a second portion of **1a** (0.128 mmol) was added, and the formation of **3a** was followed for an additional 45 min by HPLC. The similar initial rate of reaction (1.1×10^{-3} mM/min) obtained for both injections of **1a** shows that no catalyst activation or deactivation was observed during the initial 45 min of the reaction.

With regards to the mechanism of the reaction, we assume that the reaction follows the established mechanism of palladium-catalyzed coupling of aryl halides/pseudohalides and nitrogen nucleophiles (Figure 1). To our knowledge, no detailed kinetic study of the palladium-catalyzed reactions of sulfonamides with aryl halides or pseudohalides has been reported. However, kinetic and computational studies on the coupling of aryl chlorides with primary and secondary carboxamides have been reported.[8,13] These studies suggested that coordination of the amide and/or attack of the amidate on the Pd(II) oxidative-addition species (transmetalation) is the rate-limiting step in this reaction.[25] It was not apparent whether the rate-limiting step for reactions of sulfonamides is also transmetalation or a different

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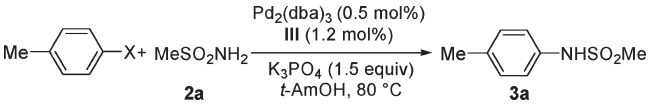
Table 4. Comparison of Initial Rates of Reactions



entry	X (mM)	**2a** (mM)	initial rates (10^{-3} mM/min)
1	ONf (0.27)	0.32	1.1
2	ONf (0.028)	0.34	1.0
3	ONf (0.27)	0.08	1.1
4	Br (0.28)	0.34	1.2

Initials rates are average of two runs.

step in the catalytic cycle, such as oxidative addition or reductive elimination.

In order to determine the rate-limiting step of the reaction, kinetic studies were performed to determine the dependence of the initial rates of reactions of aryl nonaflates with sulfonamides on the concentration of the reactants. The rates of reaction of **1a** with **2a** were obtained by following the formation of the product **3a** for the initial 20−45 min of the reaction by HPLC. No catalyst activation or deactivation was observed during this initial phase of the reaction (Figure 2).[26−28] The initial rates of reaction were found to be independent of the concentrations of both nonaflate and sulfonamide (Table 4, entries 1−3), suggesting that neither oxidative addition nor transmetalation is the rate-limiting step.[27] Similar initial rates of reaction were observed for the reactions of **1a** and *p*-bromotoluene (entries 1 and 4), further suggesting that the halide/pseudohalide is not involved in the rate-limiting step.[29] These findings taken together are consistent with reductive elimination being the rate-limiting step rather than oxidative addition or transmetalation.

The faster reaction observed with an electron-poor electrophile **1g** compared to that observed with an electron-rich electrophile **1j** (Table 2, entries 7 and 10) is also consistent with reductive elimination being the rate-limiting step for this reaction; the rate of formation of C−N bonds by reductive elimination has been observed to be faster from Pd(aryl)(amide) complexes containing electron-poor aryl groups than from Pd(aryl)(amide) complexes containing electron-rich aryl groups.[30−33] A similar reaction-rate trend of faster rate of C−X (X = O, S) bond formation has also been observed for arylpalladium complexes containing more electron-poor aryl groups.[34,35] Thus, it is reasonable to expect that the similar trend for the rate of reductive elimination will hold for Pd(aryl)(sulfonamidate) complexes.

CONCLUSIONS

In summary, the reactions of aryl and heteroaryl nonaflates with primary sulfonamides occurred in high yield in the presence of a palladium catalyst bearing a bulky, electron-rich biaryl phosphine ligand. The substrate scope of the reaction was explored in detail. Both electron-poor and electron-rich aryl nonaflates were found to be suitable electrophiles. A wide range of alkyl and aryl primary sulfonamides were demonstrated to be competent coupling partners. The inability of 2,6-disubstituted aryl nonaflates to couple under the reported reaction conditions is a major limitation of this methodology. Our preliminary experiments suggest that the reaction conditions are also applicable to the couplings of alkenyl nonaflates with sulfonamides; however, the utility may be limited as a result of instability of the coupled products, alkenyl sulfonamides, to hydrolysis. Analysis of kinetic data suggests that reductive elimination is the rate-limiting step of the reactions of aryl nonaflates with methanesulfonamide.

EXPERIMENTAL SECTION

General Methods. All palladium-catalyzed reactions were performed in a nitrogen glovebox or using Schlenk techniques under N_2/Ar atmosphere. Anhydrous grade 1,4-dioxane, *t*-AmOH, DMF, acetonitrile, THF, aryl alcohols, perfluorobutanesulfonyl fluoride, primary sulfonamides, β-tetralone, 4-phenylcyclohexanone, 2-methylcyclohexanone, $Pd_2(dba)_3$, phosphine ligands, and bases were purchased from commercial sources and were used without further purification with the exception of 4-methoxybezenesulfonamide, which was recrystallized from ethyl acetate (EtOAc). 1,4-Dioxane, *t*-AmOH, and bases were stored and used inside the glovebox. Column chromatography was performed using silica gel columns. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 or 600 MHz spectrometer, with shifts reported in parts per million downfield from tetramethylsilane and referenced to residual proton (^{1}H) or deuterated solvent (^{13}C). HPLC analyses were performed using spectroscopic grades of acetonitrile and water with either 0.1% H_3PO_4 or 0.1% $HClO_4$ as eluents. HRMS analyses were performed on a time-of-flight mass spectrometer equipped with an ESI source.

General Procedure for Synthesis of Aryl Nonaflates. A slurry of aryl alcohol (1.0 equiv) in acetonitrile (0.5 M) with 325-mesh potassium carbonate (1.5 equiv) was stirred vigorously with a magnetic stir bar. Perfluorobutanesulfonyl fluoride (1.2 equiv) was added in one portion, and the reaction progress was monitored by HPLC analysis of aliquots. If necessary, additional perfluorobutanesulfonyl fluoride was added. Upon completion of the reaction, the inorganic salts were removed by filtration over a glass frit, the solvent was removed *in vacuo*, and the residue was purified by flash column chromatography over silica gel.

4-Methylphenyl Nonaflate (1a). (Table 2, entry 1). Following the general procedure, 5.45 g of 4-methylphenol was converted to 4-methylphenyl nonaflate (**1a**). The product was isolated as a colorless liquid (18.80 g, 96% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, J = 8.4 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.4 (C), 138.1 (C), 130.3 (CH), 120.8 (CH), 21.2 (CH_3). Our carbon NMR data were consistent with the reported data, but our proton NMR data differed from the data reported in the literature.[36]

2-Methylphenyl Nonaflate (1b). (Table 2, entry 2). Following the general procedure, 1.67 g of 2-methylphenol was converted to 2-methylphenyl nonaflate (**1b**). The product was isolated as a colorless liquid (5.68 g, 94% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.22 (m, 4H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2 (C), 131.9 (CH), 130.7 (C), 127.9 (CH), 127.4 (CH), 121.0 (CH), 16.8 (CH_3). The proton and carbon NMR data for this compound were consistent with literature data.[37]

Mesityl Nonaflate (1c). (Table 2, entry 3). 325-Mesh potassium carbonate (1.53 g, 11 mmol, 1.5 equiv) was added to a solution of 1.03 g of 2,4,6-trimethylphenol (7.3 mmol, 1.0 equiv) in 14.8 mL of DMF (0.5 M), and the resultant slurry was stirred vigorously with a magnetic stir bar. Perfluorobutanesulfonyl fluoride (1.6 mL, 8.8 mmol, 1.2 equiv) was added in one portion, and the reaction progress was monitored by HPLC analysis of aliquots. After 4 h, an additional 0.92 g of potassium carbonate (0.9 equiv) and 1.6 mL of perfluorobutanesulfonyl fluoride (1.2 equiv) were added, and the reaction was allowed to proceed

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overnight. The inorganic salts were removed by filtration over a glass frit, the unpurified solution was diluted with isopropyl acetate and heptanes, and the organic solution was washed 3 times with water. The organic solvent was removed in vacuo, and the residue was purified by flash column chromatography (5−10% DCM/hexanes) to give 2.68 g (87% yield) of the title compound as a liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (s, 2H), 2.33 (s, 6H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3 (C), 137.6 (C), 130.9 (C), 130.2 (CH), 20.9 (CH_3), 17.4 (CH_3). Anal. Calcd for $C_{13}H_{11}F_9O_3S$: C, 37.33; H, 2.65. Found: C, 37.07; H, 2.36.

4-Cyanophenyl Nonaflate (1d). (Table 2, entry 4). Following the general procedure, 1.34 g of 4-cyanophenol was converted to 4-cyanophenyl nonaflate (**1d**). The product was isolated as an oil that solidified on standing (4.23 g, 94% yield) after flash chromatography over silica gel using an EtOAc/hexane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81−7.76 (m, 2H), 7.45−7.40 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.8 (C), 134.1 (CH), 122.3 (CH), 116.8 (C), 112.7 (C). The proton and carbon NMR data for this compound were consistent with literature data.[37]

4-Carboethoxyphenyl Nonaflate (1e). (Table 2, entry 5). Following the general procedure, 1.01 g of ethyl 4-hydroxybenzoate was converted to 4-carboethoxyphenyl nonaflate (**1e**). The product was isolated as a colorless liquid (2.59 g, 97% yield) after flash chromatography over silica gel using an EtOAc/hexane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16−8.11 (m, 2H), 7.37−7.32 (m, 2H), 4.39 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4 (C), 152.2 (C), 131.5 (CH), 130.4 (C), 121.1 (CH), 61.6 (CH_2), 14.6 (CH_3). The proton and carbon NMR data for this compound were consistent with literature data.[38]

3-Carboethoxyphenyl Nonaflate (1f). (Table 2, entry 6). Following the general procedure, 2.1 g of ethyl 3-hydroxybenzoate was converted to 3-carboethoxyphenyl nonaflate (**1f**). The product was isolated as a colorless liquid (5.5 g, 97% yield) after flash chromatography over silica gel using an EtOAc/hexane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dt, J = 7.7, 1.2 Hz, 1H), 7.95−7.93 (m, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.49−7.45 (m, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1 (C), 149.2 (C), 132.8 (C), 130.0 (CH), 129.1 (CH), 125.3 (CH), 122.2 (CH), 61.8 (CH_2), 14.5 (CH_3). Anal. Calcd for $C_{13}H_9F_9O_5S$: C, 34.83; H, 2.02. Found: C, 35.13; H, 1.80.

4-Nitrophenyl Nonaflate (1g). (Table 2, entry 7). Following the general procedure, 1.5 g of 4-nitrophenol was converted to 4-nitrophenyl nonaflate (**1g**). The product was isolated as a white solid (4.87 g, 97% yield) after flash chromatography over silica gel using an EtOAc/hexane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38−8.33 (m, 2H), 7.51−7.45 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.9 (C), 146.7 (C), 125.7 (CH), 122.2 (CH). Mp 67.8−69.6 °C, lit. mp 70 °C. The proton NMR data and melting point for this compound were consistent with literature data.[39]

4-Acetylphenyl Nonaflate (1h). (Table 2, entry 8). Following the general procedure, 1.5 g of 4-hydroxyacetophenone was converted to 4-acetylphenyl nonaflate (**1h**). The product was isolated as a tan solid (4.54 g, 99% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08−8.03 (m, 2H), 7.41−7.36 (m, 2H), 2.63 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4 (C), 152.3 (C), 136.4 (C), 130.2 (CH), 121.4 (CH), 27.0 (CH_3). The proton and carbon NMR data for this compound were consistent with literature data.[37]

4-Formylphenyl Nonaflate (1i). (Table 2, entry 9). Following the general procedure, 2.14 g of 4-hydroxybenzaldehyde was converted to 4-formylphenyl nonaflate (**1i**). The product was isolated as a colorless semisolid (6.82 g, 96% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, C_6D_6) δ 9.34 (s, 1H), 7.19−7.15 (m, 2H), 6.75−6.70 (m, 2H). ^{13}C NMR (101 MHz, C_6D_6) δ 188.9 (CH), 152.9 (C), 136.0 (C), 131.3 (CH), 121.9 (CH). Anal. Calcd for $C_{11}H_5F_9O_4S$: C, 32.69; H, 1.25. Found: C, 32.79; H, 0.96.

4-Methoxyphenyl Nonaflate (1j). (Table 2, entry 10). Following the general procedure, 2.75 g of 4-methoxyphenol was converted to 4-methoxyphenyl nonaflate (**1j**). The product was isolated as a colorless liquid (8.74 g, 98% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.17 (m, 2H), 6.94−6.88 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6 (C), 142.9 (C), 122.1 (CH), 114.8 (CH), 55.8 (CH_3). The proton and carbon NMR data for this compound were consistent with literature data.[37]

4-(*tert*-Butoxycarbonylamino)phenyl Nonaflate (1k). (Table 2, entry 11). Following the general procedure, 1.15 g of 4-*N*-Boc-aminophenol was converted to 4-(*tert*-butoxycarbonylamino)phenyl nonaflate (**1k**). The product was isolated as a white solid (2.68 g, 99% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.45 (m, 2H), 7.25−7.20 (m, 2H), 6.68 (s, 1H), 1.56 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0 (C), 144.3 (C), 138.1 (C), 121.7 (CH), 119.2 (CH), 81.2 (C), 28.5 (CH_3). Anal. Calcd for $C_{15}H_{14}F_9NO_5S$: C, 36.67; H, 2.87; N, 2.85. Found: C, 36.91; H, 2.68; N, 2.82. Mp 109−110 °C.

1-Naphthalenyl Nonaflate (1l). (Table 2, entry 12). Following the general procedure, 1.4 g of 1-naphthol was converted to 1-naphthalenyl nonaflate (**1l**). The product was isolated as a white solid (4.13 g, 100% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.5 Hz, 1H), 7.92−7.83 (m, 2H), 7.64 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.58 (ddd, J = 8.1, 6.9, 1.3 Hz, 1H), 7.50−7.44 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.4 (C), 134.6 (C), 128.2 (CH), 127.7 (CH), 127.6 (CH), 127.1 (CH), 126.1 (C), 124.8 (CH), 120.6 (CH), 117.6 (CH). The proton and carbon NMR data for this compound were consistent with literature data.[36]

3-Pyridyl Nonaflate (1m). (Table 2, entry 13). Following the general procedure, 1.1 g of 3-hydroxypyridine was converted to 3-pyridinyl nonaflate (**1m**). The product was isolated as a colorless liquid (4.1 g, 91% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65 (dd, J = 4.7, 1.3 Hz, 1H), 8.62 (d, J = 2.8 Hz, 1H), 7.65 (ddd, J = 8.5, 2.8, 1.3 Hz, 1H), 7.43 (dd, J = 8.5, 4.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.1 (CH), 146.6 (C), 142.5 (CH), 128.7 (CH), 124.4 (CH). HRMS (m/z): $[M + H]^+$ calcd for $C_9H_5F_9N_1O_3S_1$ 377.9841; found 377.9833.

6-Quinolyl Nonaflate (1n). (Table 2, entry 14). Following the general procedure, 1.56 g of 6-hydroxyquinoline was converted to 6-quinolinyl nonaflate (**1n**). The product was isolated as a white solid (3.69 g, 80% yield) after flash chromatography over silica gel using an acetone/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (dd, J = 4.2, 1.7 Hz, 1H), 8.28−8.22 (m, 2H), 7.80 (d, J = 2.8 Hz, 1H), 7.65 (dd, J = 9.2, 2.7 Hz, 1H), 7.55 (dd, J = 8.3, 4.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.1 (CH), 146.9 (C), 146.4 (C), 136.0 (CH), 132.0 (CH), 128.0 (C), 123.0 (CH), 122.2 (CH), 119.0 (CH). The proton and carbon NMR data for this compound were consistent with literature data.[40]

Ethyl-1-benzyl-2-methyl-5-(perfluorobutylsulfonyloxy)-1*H*-indole-3-carboxylate (1o). (Table 2, entry 15). 325 -Mesh potassium carbonate (1.8 g, 12.9 mmol, 1.6 equiv) was added to a solution of 2.5 g of ethyl 1-benzyl-2-methyl-5-(perfluorobutylsulfonyloxy)-1*H*-indole-3-carboxylate[41] (**1o**) (8.1 mmol, 1.0 equiv) in 25 mL of DMF, and the resultant slurry was stirred vigorously with a magnetic stir bar. Perfluorobutanesulfonyl fluoride (1.7 mL, 9.7 mmol, 1.2 equiv) was added in one portion, and the reaction progress was monitored by HPLC analysis of aliquots. After 3.5 h, an additional 0.25 g of potassium carbonate (0.2 equiv) and 0.3 mL of perfluorobutanesulfonyl fluoride (0.2 equiv) was added, and the reaction was allowed to proceed overnight. The inorganic salts were removed by

filtration over a glass frit, the unpurified solution was diluted with 100 mL of EtOAc and 100 mL of heptanes, and the organic solution was washed 3× with 10 mL of 10 wt % aqueous sodium chloride. The organic solution was dried over sodium sulfate, the solvent was removed in vacuo, and the residue was dissolved in acetone and absorbed onto silica gel. The desired product was eluted from the column using a gradient of EtOAc/hexane. Pure fractions (first eluting) were identified by HPLC, combined, and concentrated in vacuo to give an oil that solidified upon seeding to give 2.69 g of the title compound (56% yield). Later fractions were contaminated with ethyl 1-benzyl-5-(fluorosulfonyloxy)-2-methyl-1*H*-indole-3-carboxylate and were combined separately. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 2.5 Hz, 1H), 7.32−7.25 (m, 3H), 7.23 (d, J = 8.9 Hz, 1H), 7.08 (dd, J = 8.9, 2.5 Hz, 1H), 6.96−6.94 (m, 2H), 5.36 (s, 2H), 4.41 (q, J = 7.1 Hz, 2H), 2.75 (s, 3H), 1.45 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, CDC_3) δ 164.8 (C), 147.0 (C), 145.0 (C), 135.2 (C), 134.7 (C), 128.8 (CH), 127.7 (CH), 126.9 (C), 125.5 (CH), 115.4 (CH), 114.1 (CH), 110.3 (CH), 105.2 (C), 60.0 (CH_2), 47.1 (CH_2), 14.6 (CH_3), 12.4 (CH_3). HRMS (m/z): $[M + H]^+$ calcd for $C_{23}H_{19}F_9N_1O_5S_1$ 592.0835; found 592.0847. Mp 48.5−52.0 °C.

4-Chlorophenyl Nonaflate (1p). (Table 2, entry 1). Following the general procedure, 1.25 g of 4-chlorophenol was converted to 4-chlorophenyl nonaflate (**1p**). The product was isolated as a colorless liquid (3.73 g, 93% yield) after flash chromatography over silica gel using an EtOAc/heptane gradient. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44−7.39 (m, 2H), 7.24−7.20 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.7 (C), 133.9 (C), 130.0 (CH), 122.5 (CH). The proton and carbon NMR data for this compound were consistent with literature data.[42]

3,4-Dihydronaphthalen-2-yl Nonaflate (5). (Scheme 1). A well-stirred mixture of β-tetralone (3.0 mL, 22.7 mmol, 1.0 equiv) and perfluorobutanesulfonyl fluoride (8.0 mL, 45.4 mmol, 2.0 equiv) in THF (23 mL, 1.0 M) was cooled to an internal temperature of 10 °C and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 6.8 mL, 45.4 mmol, 2.0 equiv) was added slowly while maintaining an internal temperature below 10 °C. After addition of DBU, the ice bath was removed, and the blue solution was allowed to warm to room temperature. The reaction was allowed to proceed overnight, whereupon the reaction mixture was diluted with EtOAc (50 mL) and quenched with 20 mL of water. The layers were separated, and the organic layer was washed with water (1 × 50 mL) followed by a saturated brine wash (1 × 50 mL). The combined aqueous washes were extracted with EtOAc (1 × 30 mL). The combined organic solution was dried over Na_2SO_4 and filtered. The product was absorbed onto silica gel (dry loaded) and purified by column chromatography using a gradient eluent (100% heptanes to 10% EtOAc in heptanes) to afford 6.40 g of the title compound (66% yield) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.20 (m, 2H), 7.20−7.15 (m, 1H), 7.14−7.08 (m, 1H), 6.53 (s, 1H), 3.10 (t, J = 8.4 Hz, 2H), 2.74 (td, J = 8.4, 0.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.7 (C), 132.6 (C), 130.8 (C), 128.1 (CH), 127.2 (CH), 127.0 (CH), 126.7 (CH), 118.3 (CH), 28.8 (CH_2), 26.9 (CH_2). Anal. Calcd for $C_{14}H_9F_9O_3S$: C, 39.26; H, 2.12. Found: C, 39.55; H, 1.96.

4-Phenylcyclohex-1-enyl Nonaflate (7). (Scheme 1).[43] Phosphazene base, (*tert*-butylimino)tris(1-pyrrolidinyl)phosphorane (22.2 mL, 72.6 mmol, 1.15 equiv), was added in a dropwise manner to a cooled, well-stirred solution of perfluorobutanesulfonyl fluoride (12.53 mL, 72.6 mmol, 1.15 equiv) and 4-phenylcyclohexanone (11 g, 63.1 mmol, 1 equiv) in THF (63 mL), while the internal temperature was maintained below 10 °C. After complete addition of base, the ice bath was removed and the reaction mixture was allowed to warm to room temperature overnight. The reaction was quenched with H_2O (100 mL) and extracted with pentanes (4 × 150 mL). The combined organic phase was washed with H_2O (250 mL) and dried over $MgSO_4$. Volatiles were removed under reduced pressure, and the resulting residue was subjected to flash column chromatography using a gradient eluent (100% heptanes to 5% EtOAc in heptanes) to afford 18.2 g of the title compound (63% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.37 (m, 2H), 7.35−7.27 (m, 2H), 5.97−5.97 (m, 1H), 3.00−2.90 (m, 1H) 2.70−2.37 (m, 4H), 2.20−2.12 (m, 1H), 2.11−2.00 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.7 (C), 144.2 (C), 128.3 (CH), 126.4 (CH), 126.3 (CH), 117.9 (CH), 39.0 (CH), 31.84 (CH_2), 30.0 (CH_2), 28.2 (CH_2). Anal. Calcd for $C_{16}H_{13}F_9O_3S$: C, 42.11; H, 2.87. Found: C, 42.30; H, 2.81.

6-Methylcyclohex-1-enyl Nonaflate (9). (Scheme 1).[43] A well-stirred solution of perfluorobutanesulfonyl fluoride (1.7 mL, 9.8 mmol, 2.0 equiv) and 2-methylcyclohexanone (0.60 mL, 4.9 mmol, 1.0 equiv) in THF (5 mL) was cooled −20 °C. Phosphazene base, 1-(*tert*-butylimino)-1,1,3,3,3-penta-kis(dimethylamino)-1λ^5,3λ^5-diphosphazene (2.0 M in THF) (4.9 mL, 9.8 mmol, 2.0 equiv), was added in a dropwise manner while the internal temperature was maintained below −20 °C. After complete addition of base, the reaction was allowed to stir for 72 h at −20 °C. The reaction was quenched with H_2O (50 mL) and extracted with pentanes (4 × 125 mL). The combined organic phase was washed with H_2O (50 mL) and dried over $MgSO_4$. Volatiles were removed under reduced pressure, and the resulting residue was subjected to flash column chromatography using a gradient eluent (100% heptanes to 5% EtOAc in heptanes) to afford 1.4 g of the title compound (73% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddd, 1H, J = 3.2, 1.5, 1.5 Hz.), 2.62−2.53 (m, 1H), 2.24−2.18 (m, 2H), 2.01−1.92 (m, 1H), 1.75−1.59 (m, 2H), 1.55−1.47 (m, 1H), 1.19 (d, J = 7.0 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1 (C), 118.0 (CH), 32.8 (CH), 31.8 (CH_2), 24.8 (CH_2), 19.5 (CH_2), 18.1 (CH_3). Anal. Calcd for $C_{11}H_{11}F_9O_3S$: C, 33.51; H, 2.81. Found: C, 33.39; H, 2.76.

General Procedure for Pd-Catalyzed Sulfonamidation of Aryl Nonaflates (Table 1). In a glovebox, a 40-mL reaction vial equipped with a magnetic stir bar and fitted with a Teflon screw cap septum was charged with *p*-methylbenzene nonaflate (**1a**) (0.78 mmol), methanesulfonamide (**2a**) (0.92 mmol), Cs_2CO_3 or K_3PO_4[44] or 325-mesh K_2CO_3 (1.15 mmol), $Pd_2(dba)_3$ (3.9 μmol), and phosphine ligand (9.4 μmol). Solvent (2.5 mL) was added with a syringe. The reaction vial was placed into a metal heating block, the temperature was raised to 80 °C, and the reaction mixture was stirred for 15 h. The reaction mixture was removed from the heating block, cooled to room temperature, brought outside the glovebox, filtered through a Whatman 0.2 μm PTFE filter, rinsed with solvent (∼4−6 mL), and was collected in a tared 25-mL Erlenmeyer flask. The weight of filtered solution (W_{prod}) was recorded. A portion (∼ 0.6−1.1 g) of the solution was weighed into a tared 50-mL volumetric flask (W_{sample}), diluted to 50 mL with acetonitrile and was injected into an HPLC instrument. The area corresponding to the product **3a** was recorded (A_{prod}).

Assay Yield Calculation. The product **3a** obtained in entry 4, Table 1 was isolated by flash column chromatography using 20−35% EtOAc in heptanes as eluent; **3a** (0.0165 g) was weighed into a 50-mL volumetric flask (W_{std}), dissolved in 50 mL acetonitrile, and injected into a HPLC instrument. The area corresponding to the product was recorded (A_{std}). The assay yield of **3a** in entries 1−11, Table 1 was determined by using the following formula.

$$\text{assay yield } (\%) = \frac{A_{prod} \times W_{prod} \times W_{std} \times 100}{A_{std} \times W_{sample} \times \text{theroretical yield } (g)}$$

General Procedure for Pd-Catalyzed Sulfonamidation of Aryl Nonaflates (Tables 2 and 3 and eq 1). In a glovebox, a 40-mL reaction vial equipped with a magnetic stir bar and fitted with Teflon screw cap was charged with K_3PO_4 (1.1 equiv), $Pd_2(dba)_3$ (0.005 equiv), and ligand **III** (0.012 equiv). *t*-AmOH (1.5 mL) was added, the vial was placed on a metal heating block, the temperature was raised to 80 °C, and the mixture was stirred for 30 min.[45] The vial was removed from the heating block and was charged with sulfonamide (1.2 equiv) and aryl nonaflate (1.0 equiv). Additional *t*-AmOH was added to make the reaction concentration 0.29 M with respect to the limiting reagent,

aryl nonaflate. The reaction vial was then returned to the metal heating block and stirred for 15 h at 80 °C.[46] The reaction vial was removed from the heating block, brought outside the glovebox, diluted with EtOAc, and washed with water. The layers were separated, and the organic layer was washed with brine and concentrated *in vacuo*. The product was isolated via flash column chromatography.

4-Methyl-*N*-*p*-tolylbenzenesulfonamide (3b). (Table 2, entry 1). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 4-tolylsulfonamide (**2b**) (0.26 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.6 mL) was stirred at 80 °C for 16 h. The crude product was purified via flash column chromatography over two columns (10−40% EtOAc/heptanes, then 1−5% EtOAc/DCM) to provide the title compound as a white solid (0.30 g, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.58 (m, 2H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 6.96−6.91 (m, 2H), 6.40 (s, 1H), 2.37 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.3 (C), 135.7 (C), 134.9 (C), 133.4 (C), 129.5 (CH) 129.2 (CH), 126.9 (CH), 121.9 (CH), 21.8 (CH_3), 21.1 (CH_3). HRMS (*m*/*z*): $[M + Na]^+$ calcd for $C_{14}H_{15}N_1O_2S_1Na$ 284.0716, found 284.0718. Mp 116−117.5 °C, lit. mp 118−118.7 °C.[47]

4-Methyl-*N*-*o*-tolylbenzenesulfonamide (3c). (Table 2, entry 2). Following the general procedure, a mixture of 2-methylphenyl nonaflate (**1b**) (0.50 g, 1.28 mmol), 4-tolylsulfonamide (**2b**) (0.26 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0058 g, 6.3 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.4 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (10−40% EtOAc/hexanes) to provide the title compound as a white solid (0.32 g, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.58 (m, 2H), 7.30 (d, *J* = 7.7 Hz, 1H), 7.22−7.18 (m, 2H), 7.15−7.09 (m, 1H), 7.08−7.03 (m, 2H), 6.40 (br s, 1H), 2.38 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.4 (C), 136.3(C), 134.1 (C), 130.9(C), 130.4 (CH), 129.3 (CH), 126.8 (CH), 126.6 (CH), 125.9 (CH), 124.0 (CH), 21.8 (CH_3), 17.9 (CH_3). HRMS (*m*/*z*): $[M - H]^-$ calcd for $C_{14}H_{14}N_1O_2S_1$ 260.0751; found, 260.0749. Mp 105−107 °C, lit. mp 108−109 °C.[48]

***N*-(4-Cyanophenyl)-4-methylbenzenesulfonamide (3e).** (Table 2, entry 4). Following the general procedure, a mixture of 4-cyanophenyl nonaflate (**1d**) (0.51 g, 1.28 mmol), 4-tolylsulfonamide (**2b**) (0.26 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 16 h. The crude product was purified via flash column chromatography (0−30% EtOAc/hexanes) to provide the title compound as a white solid (0.31 g, 89%). ^{1}H NMR (400 MHz, DMSO) δ 10.96 (s, 1H), 7.75−7.68 (m, 2H), 7.69−7.65 (m, 2H), 7.35 (app d, *J* = 8.4 Hz, 2H), 7.25−7.20 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 143.3 (C), 141.7 (C), 135.6 (C), 133.1 (CH), 129.4 (CH), 126.2 (CH), 118.2 (C), 117.9 (CH), 104.9 (C), 21.0 (CH_3). HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{14}H_{13}N_2O_2S_1$ 273.0692; found 273.0694. Mp 183.2−184.4 °C, lit. mp 180 °C.[49]

Ethyl-4-(4-methylphenylsulfonamido)benzoate (3f). (Table 2, entry 5). Following the general procedure, a mixture of 4-carboethoxyphenyl nonaflate (**1e**) (0.5 g, 1.11 mmol), 4-tolylsulfonamide (**2b**) (0.23 g, 1.34 mmol), K_3PO_4 (0.26 g, 1.23 mmol), $Pd_2(dba)_3$ (0.0051 g, 5.6 μmol) and **III** (0.0057 g, 13 μmol) in *t*-AmOH (3.9 mL) was stirred at 80 °C for 4 h. The crude product was purified via flash column chromatography (0−2% MeOH/DCM) to provide the title compound as an off-white solid (0.33 g, 92%). ^{1}H NMR (400 MHz, DMSO) δ 10.77 (s, 1H), 7.82−7.7 (m, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.26−7.16 (m, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.31 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 164.4 (C), 143.0 (C), 141.8 (C), 135.8 (C), 130.0 (CH), 129.3 (CH), 126.2 (CH), 124.1 (C), 117.6 (CH), 60.3 (CH_2), 21.0 (CH_3), 14.3 (CH_3). HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{16}H_{18}N_1O_4S_1$ 320.0951; found 320.0940. Mp 205−206 °C, lit. mp 205−206 °C.[50]

Ethyl-3-(4-methylphenylsulfonamide)benzoate (3g). (Table 2, entry 6). Following the general procedure, a mixture of 3-carboethoxyphenyl nonaflate (**1f**) (0.50 g, 1.11 mmol), 4-tolylsulfonamide (**2b**) (0.23 g, 1.34 mmol), K_3PO_4 (0.26 g, 1.23 mmol), $Pd_2(dba)_3$ (0.0051 g, 5.6 μmol) and **III** (0.0057 g, 13 μmol) in *t*-AmOH (3.8 mL) was stirred at 80 °C for 16 h. The crude product was purified via flash column chromatography over two columns (10−40% acetone/heptanes, then 20−40% EtOAc/heptanes) to provide the title compound as a white solid (0.31 g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.71−7.65 (m, 3H), 7.41 (ddd, *J* = 8.1, 2.3, 1.1 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.22−7.17 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5 (C), 143.7 (C), 136.7 (C), 135.6 (C), 131.3 (C), 129.4 (CH), 129.1 (CH), 127.0 (CH), 125.8 (CH), 124.9 (CH), 121.7 (CH), 61.4 (CH_2), 21.8 (CH_3), 14.6 (CH_3). HRMS (*m*/*z*): $[M - H]^-$ calcd for $C_{16}H_{16}N_1O_4S_1$ 318.0806; found 318.0808. Mp 90−92.3 °C.

4-Methyl-*N*-(4-nitrophenyl)benzenesulfonamide (3h). (Table 2, entry 7). Following the general procedure, a mixture of 4-nitrophenyl nonaflate (**1g**) (0.50 g, 1.19 mmol), 4-tolylsulfonamide (**2b**) (0.24 g, 1.42 mmol), K_3PO_4 (0.28 g, 1.31 mmol), $Pd_2(dba)_3$ (0.0027 g, 2.9 μmol) and **III** (0.0030 g, 7.1 μmol) in *t*-AmOH (4.1 mL) was stirred at 80 °C for 1 h. The crude product was purified via flash column chromatography (0−30% EtOAc/heptanes) to provide the title compound as an off-white solid (0.32 g, 92%). ^{1}H NMR (400 MHz, DMSO) δ 11.19 (s, 1H), 8.15−8.05 (m, 2H), 7.74 (app d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.32−7.26 (m, 2H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 144.9 (C), 144.7 (C), 143.1 (C), 136.8 (C), 130.7 (CH), 127.5 (CH), 126.1 (CH), 118.6 (CH), 22.3 (CH_3). HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{13}H_{13}N_2O_4S_1$ 293.0591; found 293.0590. Mp 191.7−193 °C, lit. mp 193 °C.[51]

***N*-(4-Acetylphenyl))-4-methylbenzenesulfonamide (3i).** (Table 2, entry 8) Following the general procedure, a mixture of 4-acetylphenyl nonaflate (**1h**) (0.537 g, 1.29 mmol), 4-tolylsulfonamide (**2b**) (0.20 g, 1.17 mmol), K_3PO_4 (0.27 g, 1.29 mmol), $Pd_2(dba)_3$ (0.0054 g, 5.9 μmol) and **III** (0.0060 g, 14 μmol) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (5−40% EtOAc/CH_2Cl_2) to provide the title compound as a white solid (0.299 g) which was 98 wt % by ^{1}H NMR (0.292 g, 86%), the major impurity being acetone. ^{1}H NMR (400 MHz, DMSO) δ 10.78 (br s, 1H), 7.82−7.77 (m, 2H), 7.71−7.66 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.19−7.14 (m, 2H), 2.46 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 195.5 (C), 143.1 (C), 141.7 (C), 135.8 (C), 131.3 (C), 129.3 (CH), 129.3 (CH), 126.2 (CH), 117.3 (CH), 26.4 (CH_3), 21.0 (CH_3). HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{15}H_{16}N_1O_3S_1$ 290.0845; found 290.0846. Mp 200.6−202.5 °C, lit. mp 203−204 °C.[52]

***N*-(4-Formylphenyl))-4-methylbenzenesulfonamide (3j).** (Table 2, entry 9). Following the general procedure, a mixture of 4-formylphenyl nonaflate (**1i**) (0.51 g, 1.26 mmol), 4-tolylsulfonamide (**2b**) (0.18 g, 1.05 mmol), K_3PO_4 (0.24 g, 1.16 mmol), $Pd_2(dba)_3$ (0.0048 g, 5.2 μmol) and **III** (0.0054 g, 13 μmol) in *t*-AmOH (3.6 mL) was stirred at 80 °C for 16 h. The crude product was purified via flash column chromatography (5−85% EtOAc/CH_2Cl_2) to provide the title compound as a white solid (0.24 g, 82%). ^{1}H NMR (400 MHz, DMSO) δ 10.92 (br s, 1H), 9.76 (s, 1H), 7.75−7.72 (m, 2H), 7.72−7.68 (m, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 7.26−7.22 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 190.8 (CH), 143.4 (C), 143.1 (C), 135.8 (C), 130.9 (C), 130.7 (CH), 129.5 (CH), 126.4 (CH), 117.7 (CH), 21.2 (CH_3). HRMS (*m*/*z*): $[M - H]^-$ calcd for $C_{14}H_{12}N_1O_3S_1$ 274.0543; found 274.0543. Mp 190.8−191.5 °C, lit. mp 188−188.5 °C.[53]

***N*-(4-Methoxyphenyl)-4-methylbenzenesulfonamide (3k).** (Table 2, entry 10). Following the general procedure, a mixture of 4-methoxyphenyl nonaflate (**1j**) (0.50 g, 1.23 mmol), 4-tolylsulfonamide

(**2b**) (0.25 g, 1.48 mmol), K_3PO_4 (0.29 g, 1.35 mmol), $Pd_2(dba)_3$ (0.0085 g, 9.3 μmol) and **III** (0.0094 g, 22 μmol) in *t*-AmOH (4.2 mL) was stirred at 90 °C for 15 h. The crude product was purified via flash column chromatography (0−20% EtOAc/heptanes) to provide the title compound as a white solid (0.31 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58−7.52 (m, 2H), 7.20 (app d, J = 8.0 Hz, 2H), 6.97−6.91 (m, 2H), 6.78−6.72 (m, 2H), 6.15 (s, 1H), 3.75 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4 (C), 143.2 (C), 135.6 (C), 129.2 (CH), 128.6 (C), 127.0 (CH), 125.0 (CH), 114.1 (CH), 55.5 (CH_3), 21.8 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{14}H_{14}N_1O_3S_1$ 276.0700; found 276.0702. Mp 111.9−113.1 °C, lit. mp 112 °C.[54]

***tert*-Butyl-4-(4-methylphenylsulfonamide)phenylcarbamate (3l).** (Table 2, entry 11). Following the general procedure, a mixture of 4-*tert*-butoxycarbonylaminophenyl nonaflate (**1k**) (0.50 g, 1.02 mmol), 4-tolylsulfonamide (**2b**) (0.21 g, 1.22 mmol), K_3PO_4 (0.24 g, 1.12 mmol), $Pd_2(dba)_3$ (0.0047 g, 5.1 μmol) and **III** (0.0052 g, 12 μmol) in *t*-AmOH (3.5 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−20% EtOAc/heptanes) to provide the title compound as a white solid (0.34 g, 92%). ^{1}H NMR (400 MHz, DMSO) δ 9.88 (s, 1H), 9.22 (s, 1H), 7.58−7.52 (m, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.8 Hz, 2H), 6.94−6.88 (m, 2H), 2.32 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, DMSO) δ 152.1 (C), 142.4 (C), 136.0 (C), 135.7 (C), 131.2 (C), 129.0 (CH), 126.2 (CH), 121.2 (CH), 118.3 (CH), 78.7 (C), 28.1 (CH_3), 21.0 (CH_3). HRMS (m/z): $[M + Na]^+$ calcd for $C_{18}H_{22}N_2O_4S_1Na$ 385.1193; found 385.1191. Mp 167−168 °C.

4-Methyl-*N*-(naphthalene-1-yl)benzenesulfonamide (3m). (Table 2, entry 12). Following the general procedure, a mixture of naphthalene-1-yl nonaflate (**1l**) (0.50 g, 1.17 mmol), 4-tolylsulfonamide (**2b**) (0.24 g, 1.41 mmol), K_3PO_4 (0.27 g, 1.29 mmol), $Pd_2(dba)_3$ (0.0054 g, 5.9 μmol) and **III** (0.0060 g, 14 μmol) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−10% EtOAc/hexanes) to provide the title compound as a white solid (0.34 g, 95%).^{1}H NMR (400 MHz, DMSO) δ 10.14 (s, 1H), 8.02 (dd, J = 8.3, 0.9 Hz, 1H), 7.86 (dd, J = 8.3, 1.0 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H), 7.60−7.53 (m, 2H), 7.48−7.40 (m, 2H), 7.37 (dd, J = 8.3, 7.5 Hz, 1H), 7.28 (app d, J = 8.3 Hz, 2H), 7.12 (dd, J = 7.4, 1.1 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 142.4 (C), 136.7 (C), 133.3 (C), 132.0 (C), 129.0 (CH), 128.8 (C), 127.4 (CH), 126.2 (CH), 126.0 (CH), 125.7 (CH), 125.5 (CH), 125.0 (CH), 122.7 (CH), 122.3 (CH), 21.1 (CH_3). HRMS (m/z): $[M + Na]^+$ calcd for $C_{17}H_{15}N_1O_2S_1Na$ 320.0716; found 320.0726. Mp 156.3−158.2 °C, lit. mp 157−158 °C.[55]

4-Methyl-*N*-(pyridine-3-yl)benzenesulfonamide (3n). (Table 2, entry 13). Following the general procedure, a mixture of pyridine-3-yl nonaflate (**1m**) (1.0 g, 2.65 mmol), 4-tolylsulfonamide (**2b**) (0.50 g, 2.92 mmol), Cs_2CO_3 (1.04 g, 3.18 mmol), $Pd_2(dba)_3$ (0.049 g, 54 μmol) and **III** (0.054 g, 127 μmol) in *t*-AmOH (8.5 mL) was stirred at 90 °C for 20 h. The unpurified mixture was diluted with 40 mL of THF and 5 mL of saturated sodium chloride solution, and the pH of the aqueous solution was adjusted to neutral with 3.2 mL of 1 M HCl solution. After separation, the organic solution was concentrated to dryness in vacuo. Heptane was added and removed in vacuo. The residue was dissolved in THF and absorbed onto silica gel. The desired product was purified by flash column chromatography using a gradient elution (50−100% EtOAc/hexanes). Product-containing fractions were combined and concentrated in vacuo to give a white solid. This solid was slurried with 25% EtOAc/heptane (10 mL), filtered and dried in a vacuum oven at 50 °C to obtain the title compound as a white solid (0.53 g, 80%). ^{1}H NMR (400 MHz, DMSO) δ 10.46 (br s, 1H), 8.25 (dd, J = 2.6, 0.6 Hz, 1H), 8.22 (dd, J = 4.7, 1.4 Hz, 1H), 7.66−7.59 (m, 2H), 7.47 (ddd, J = 8.3, 2.7, 1.5 Hz, 1H), 7.36−7.32 (m, 2H), 7.26 (ddd, J = 8.3, 4.7, 0.7 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 144.6 (CH), 143.0 (C), 141.1 (CH), 135.6 (C), 133.9 (C), 129.3 (CH), 126.7 (CH), 126.2 (CH), 123.5 (CH), 21.0 (CH_3). HRMS (m/z): $[M + H]^+$ calcd for $C_{12}H_{13}N_2O_2S_1$ 249.0692; found 249.0696. Mp 191.5−193 °C, lit. mp 191−192 °C.[56]

4-Methyl-*N*-(quinolin-6-yl)benzenesulfonamide (3o). (Table 2, entry 14). Following the general procedure, a mixture of quinolin-6-yl nonaflate (**1n**) (0.50 g, 1.17 mmol), 4-tolylsulfonamide (**2b**) (0.18 g, 1.05 mmol), K_3PO_4 (0.27 g, 1.29 mmol), $Pd_2(dba)_3$ (0.0054 g, 5.9 μmol) and **III** (0.0059 g, 14 μmol) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (35−70% EtOAc/heptanes) to provide the title compound as a white solid (0.30 g, 86%). ^{1}H NMR (400 MHz, DMSO) δ 10.62 (br s, 1H), 8.74 (dd, J = 4.2, 1.6 Hz, 1H), 8.23 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 9.0 Hz, 1H), 7.73−7.68 (m, 2H), 7.61 (d, J = 2.4 Hz, 1H), 7.50 (dd, J = 9.0, 2.5 Hz, 1H), 7.43 (dd, J = 8.3, 4.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 148.8 (CH), 144.2 (C), 142.9 (C), 135.9 (C), 135.3 (C), 134.8 (CH), 129.6 (CH), 129.2 (CH), 127.7 (C), 126.3 (CH), 123.0 (CH), 121.5 (CH), 114.8 (CH), 21.0 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{16}H_{13}N_2O_2S_1$ 297.0703; found 297.0707. Mp 194−197 °C, lit. mp 196−197 °C.[57]

Ethyl 1-Benzyl-2-methyl-5-(4-methylphenylsulfonamido)-1*H*-indole-3-carboxylate (3p). (Table 2, entry 15). Following the general procedure, a mixture of ethyl 1-benzyl-2-methyl-5-(perfluorobutylsulfonyloxy)-1*H*-indole-3-carboxylate (**1o**) (0.50 g, 0.85 mmol), 4-tolylsulfonamide (**2b**) (0.17 g, 1.01 mmol), K_3PO_4 (0.20 g, 0.93 mmol), $Pd_2(dba)_3$ (0.0075 g, 8.2 μmol) and **III** (0.0086 g, 20 μmol) in *t*-AmOH (2.9 mL) was stirred at 90 °C for 15 h. The crude product was purified via flash column chromatography (0−3% MeOH/CH_2Cl_2). The white solid obtained was stirred in a mixture of EtOAc (5 mL) and hexanes (15 mL) at room temperature for 30 min, filtered through a Buchner funnel, and washed with hexanes (5 mL) to obtain the title compound as a white solid (0.34 g, 88%). ^{1}H NMR (400 MHz, DMSO) δ 9.94 (s, 1H), 7.74 (d, J = 2.1 Hz, 1H), 7.62−7.55 (m, 2H), 7.35 (d, J = 8.8 Hz, 1H), 7.32−7.19 (m, 5H), 7.00−6.93 (m, 2H), 6.88 (dd, J = 8.7, 2.1 Hz, 1H), 5.43 (s, 2H), 4.24 (q, J = 7.1 Hz, 2H), 2.63 (s, 3H), 2.30 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 163.9 (C), 145.3 (C), 142.2 (C), 136.4 (C), 132.9 (C), 131.3 (C), 128.9 (CH), 128.2 (CH), 126.8 (CH), 126.2 (CH), 125.7 (C), 125.6 (CH), 116.6 (CH), 113.2 (CH), 110.2 (CH), 102.9 (C), 58.8 (CH_2), 45.8 (CH_2), 20.9 (CH_3), 14.4 (CH_3), 11.8 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{26}H_{25}N_2O_4S_1$ 461.1541; found 461.1537. Mp 216.5−220.0 °C.

***N*-(4-Chlorophenyl)-4-methylbenzenesulfonamide (3q).** (Table 2, entry 16). Following the general procedure, a mixture of 4-chlorophenyl nonaflate (**1p**) (0.58 g, 1.41 mmol), 4-tolylsulfonamide (**2b**) (0.22 g, 1.28 mmol), K_3PO_4 (0.30 g, 1.34 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.2 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (20−50% EtOAc/hexanes) to provide the title compound as a white solid (0.31 g, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.60 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.21−7.16 (m, 2H), 7.02−6.97 (m, 2H), 6.66 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8 (C), 135.3 (C), 134.7 (C), 130.6 (C), 129.5 (CH), 129.1 (CH), 126.9 (CH), 122.7 (CH), 21.8 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{13}H_{11}N_1O_2S_1Cl_1$ 280.0205; found 280.0206. Mp 115−118 °C, lit. mp 118−119 °C.[58]

***N*-*p*-Tolylmethanesulfonamide (3a).** (Table 3, entry 1). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), methanesulfonamide (**2a**) (0.15 g, 1.54 mmol), K_3PO_4 (0.41 g, 1.92 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.4 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−25% EtOAc/hexanes) to provide the title compound as a white solid (0.22 g, 94%). ^{1}H NMR (400 MHz, $CDlL_3$) δ 7.22−7.15 (m, 4H), 7.03−6.89 (br s, 1H), 3.02 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (101 MHz,

$CDCl_3$) δ 135.1 (CH), 133.6 (CH), 129.8 (CH), 121.3 (CH), 39.1 (CH_3), 21.1 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_8H_{10}N_1O_2S_1$ 184.0438; found 184.0440. Mp 101.5−102.8 °C, lit. mp 102−103.5 °C.[47]

***N*-*p*-Tolylcyclopropanesulfonamide (3r).** (Table 3, entry 2). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), cyclopropanesulfonamide (**2c**) (0.19 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.065 g, 15 μmol) in *t*-AmOH (4.4 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−30% acetone/heptanes) to provide the title compound as a white solid (0.27 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19−7.13 (m, 4H), 6.55 (br s, 1H), 2.47 (tt, J = 8.0 Hz, 4.8 Hz, 1H), 2.34 (s, 3H), 1.19−1.13 (m, 2H), 0.97−0.91 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7 (C), 134.1 (C), 130.1 (CH), 122.6 (CH), 29.5 (CH), 20.7 (CH_3), 5.3 (CH_2). HRMS (m/z): $[M + Na]^+$ calcd for $C_{10}H_{13}N_1O_2S_1Na$ 234.0559; found 234.0557. Mp 94.4−96.1 °C, lit. mp 80 °C.[59,60]

1-Methyl-*N*-*p*-tolylcyclopropane-1-sulfonamide (3s). (Table 3, entry 3). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 1-methylcyclopropane-1-sulfonamide (**2d**) (0.21 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0120 g, 15 μmol) in *t*-AmOH (4.4 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−20% acetone/heptanes) to provide the title compound as a white solid (0.26 g, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18−7.13 (m, 2H), 7.10 (app d, J = 8.5 Hz, 2H), 6.86 (br s, 1H), 2.32 (s, 3H), 1.50 (s, 3H), 1.31−1.28 (m, 2H), 0.71−0.64 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.8 (C), 134.1 (C), 129.5 (CH), 122.0 (CH), 35.8 (C), 21.1 (CH_3), 18.8 (CH_3), 12.9 (CH_2). $[M - H]^-$ calcd for $C_{11}H_{14}N_1O_2S_1$ 224.0751; found 224.0750. Mp 116−117.7 °C.

2-Methyl-*N*-*p*-tolylpropane-2-sulfonamide (3t). (Table 3, entry 4). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 2-methylpropane-2-sulfonamide (**2e**) (0.21 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.012 g, 13 μmol) and **III** (0.013 g, 31 μmol) in *t*-AmOH (4.4 mL) was stirred at 100 °C for 15 h. The crude product was purified via flash column chromatography (0−15% acetone/heptanes) to provide the title compound as a white solid (0.25 g, 86%).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.15 (m, 2H), 7.08 (app d, J = 8.5 Hz, 2H), 6.87 (s, 1H), 2.30 (s, 3H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5 (C), 133.9 (C), 129.5 (CH), 120.5 (CH), 61.9 (C), 25.1 (CH_3), 21.0 (CH_3). HRMS (m/z): $[M + Na]^+$ calcd for $C_{11}H_{17}N_1O_2S_1Na$ 250.0872; found 250.0866. Mp 147.2−149.2 °C.

2,4,6-Trimethyl-*N*-*p*-tolylbenzenesulfonamide (3u). (Table 3, entry 5). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 2,4,6-trimethylbenzenesulfonamide (**2f**) (0.31 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 16 h. The crude product was purified via flash column chromatography (CH_2Cl_2) to provide the title compound as a white solid (0.31 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (d, J = 8.1 Hz, 2H), 6.94 (d, J = 0.4 Hz, 2H), 6.92−6.87 (m, 2H), 6.84 (br s, 1H), 2.63 (s, 6H), 2.31 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1 (C), 138.9 (C), 134.8 (C), 133.3 (C), 133.0 (C), 131.6 (CH), 129.4 (CH), 121.7 (CH), 23.3 (CH_3), 21.2 (CH_3), 21.1 (CH_3). HRMS (m/z): $[M + H]^+$ calcd for $C_{16}H_{20}NO_2S_1$ 290.1209; found 290.1211. Mp 119.8−121.8 °C.

4-Methoxy-*N*-*p*-tolylbenzenesulfonamide (3v). (Table 3, entry 6). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 4-methoxybenzenesulfonamide (**2g**) (0.29 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−35% EtOAc/heptanes) to provide the title compound as a white solid (0.33 g, 94%). ^{1}H NMR (400 MHz, DMSO) δ 9.93 (s, 1H), 7.65−7.61 (m, 2H), 7.05−6.98 (m, 4H), 6.96−6.92 (m, 2H), 3.77 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 161.6 (C), 134.7 (C), 132.6 (C), 130.6 (C), 129.0 (CH), 128.3 (CH), 119.9 (CH), 113.8 (CH), 55.5 (CH_3), 20.4 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{14}H_{14}N_1O_3S_1$ 276.0700; found 276.0704. Mp 94.6−96.6 °C, lit. mp 109.5−110 °C.[61,62]

4-Nitro-*N*-*p*-tolylbenzenesulfonamide (3w). (Table 3, entry 7). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 4-nitrobenzenesulfonamide (**2h**) (0.31 g, 1.54 mmol), Cs_2CO_3 (0.46 g, 1.41 mmol), $Pd_2(dba)_3$ (0.018 g, 20 μmol) and **III** (0.020 g, 47 μmol) in *t*-AmOH (4.0 mL) was stirred at 100 °C for 22 h. The crude product was purified via flash column chromatography (0−40% EtOAc/heptanes) to provide the title compound as a yellow solid. This solid was repurified by column chromatography (0−40% EtOAc/heptanes) to obtain the title compound as a yellow solid (0.31 g, 82%). ^{1}H NMR (400 MHz, DMSO) δ 10.40 (s, 1H), 8.39−8.30 (m, 2H), 7.97−7.89 (m, 2H), 7.04 (app d, J = 8.2 Hz, 2H), 6.99−6.93 (m, 2H), 2.18 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 149.1 (C), 144.3 (C), 133.63 (C), 133.59 (C), 129.2 (CH), 127.7 (CH), 124.1 (CH), 120.8 (CH), 20.4 (CH_3). HRMS (m/z): $[M + Na]^+$ calcd for $C_{13}H_{12}N_2O_4S_1Na$ 315.0410; found 315.0396. Mp 181.6−183 °C, lit. mp 184−184.5 °C.[63]

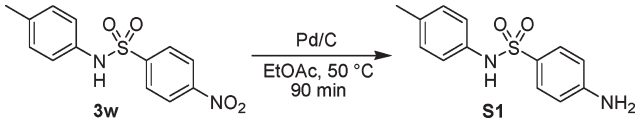
***N*-*p*-Tolyl-4-(trifluoromethyl)bezenesulfonamide (3x).** (Table 3, entry 8). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 4-(trifluoromethyl)benzenesulfonamide (**2i**) (0.35 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.018 g, 20 μmol) and **III** (0.020 g, 47 μmol) in *t*-AmOH (4.4 mL) was stirred at 100 °C for 15 h. The crude product was purified via flash column chromatography (0−15% EtOAc/hexanes) to provide the title compound as a white solid (0.37 g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.2 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H), 7.10−7.07 (m, 3H), 7.03−6.97 (m, 2H), 2.32 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.5 (C), 136.2 (C), 134.5 (C, q, J = 33.2 Hz), 132.9 (C), 130.0 (CH), 127.7 (CH), 126.1 (CH, q, J = 4.5 Hz), 123.1 (CF_3, q, J = 273.3 Hz), 122.7 (CH), 20.8 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{14}H_{11}N_1O_2F_3S_1$ 314.0468; found 314.0471. Mp 123.7−124.6 °C.

4-Hydroxy-*N*-*p*-tolylbenzenesulfonamide (3y). (Table 3, entry 9). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 4-hydroxybenzenesulfonamide (**2j**) (0.27 g, 1.54 mmol), K_3PO_4 (0.41 g, 1.92 mmol), $Pd_2(dba)_3$ (0.023 g, 25 μmol) and **III** (0.026 g, 61 μmol) in t-AmOH (4.4 mL) was stirred at 90 °C for 15 h. The crude product was purified via flash column chromatography (0−25% EtOAc/heptanes) to provide the title compound as pale yellow oil. EtOAc (2 mL) and hexanes (10 mL) were added to the oil and stirred for 6 h at room temperature, and the solvent was removed using a syringe. The white solid obtained was dried in a vacuum oven at 60 °C over 60 h to afford the title compound (0.28 g, 83%). ^{1}H NMR (400 MHz, DMSO) δ 10.38 (s, 1H), 9.85 (s, 1H), 7.56−7.51 (m, 2H), 7.01 (d, J = 8.3 Hz, 2H), 6.97−6.92 (m, 2H), 6.85−6.79 (m, 2H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.4 (C), 134.8 (C), 132.4 (C), 128.96 (C), 128.92 (CH), 128.5 (CH), 119.8 (CH), 115.0 (CH), 20.4 (CH_3). HRMS (m/z): $[M - H]^-$ calcd for $C_{13}H_{12}N_1O_3S_1$ 262.0543; found 262.0545. Mp 150−153 °C, lit. mp 151−152 °C.[64]

4-(*p*-Tolylamino)benzenesulfonamide (4). (Table 3, entry 10). Following the general procedure, a mixture of 4-methylphenyl nonaflate (**1a**) (0.50 g, 1.28 mmol), 4-aminobenzenesulfonamide (**2k**) (0.27 g, 1.54 mmol), K_3PO_4 (0.30 g, 1.41 mmol), $Pd_2(dba)_3$ (0.0059 g, 6.4 μmol) and **III** (0.0065 g, 15 μmol) in *t*-AmOH (4.4 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (0−5% MeOH/CH_2Cl_2) to provide the title compound as an off-white solid (0.28 g, 82%). ^{1}H NMR (400 MHz, DMSO)

δ 8.54 (s, 1H), 7.63−7.57 (m, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.07−7.04 (m, 2H), 7.04 (s, 2H), 7.02−6.99 (m, 2H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 147.0 (C), 138.2 (C), 132.4 (C), 130.4 (C), 129.3 (CH), 127.0 (CH), 119.3 (CH), 113.1 (CH), 20.5 (CH_3). HRMS (*m*/*z*): $[M + H]^+$ calcd for $C_{13}H_{15}N_2O_2S_1$ 263.0849; found 263.0846. Mp 162−165 °C.

To confirm that the product of this reaction was structure **4** and not the regioisomeric product, **S1** was prepared independently by hydrogenation of **3w**. Proton NMR data and melting point for **S1** were consistent with literature data and **S1** and **4** were distinct compounds by ^{1}H and ^{13}C NMR as well as by melting point.



4-Nitro-*N*-*p*-tolylbenzenesulfonamide (**3w**) (0.050 g, 0.172 mmol), Pd/C (5 mg) and EtOAc (2 mL) were charged to a 20-mL pressure reactor, the temperature was raised to 50 °C, and the reaction mixture was stirred under a hydrogen atmosphere (40 psig). The reaction progress was monitored by HPLC. Greater than 99% consumption of **3w** was observed after 90 min. The reaction mixture was cooled to the room temperature, filtered through a 0.2 μm PTFE syringe filter, rinsed with EtOAc (1 mL), and concentrated *in vacuo* to obtain **S1** as white solid. ^{1}H NMR (400 MHz, DMSO) δ 9.65 (s, 1H), 7.36−7.31 (m, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.96−6.90 (m, 2H), 6.52−6.47 (m, 2H), 5.93 (s, 2H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 152.1 (C), 135.3 (C), 132.0 (C), 128.8 (CH), 128.2 (CH), 124.0 (C), 119.5 (CH), 112.1 (CH), 20.4 (CH_3). Mp 185.8−188 °C, lit. mp 190−190.5 °C.[65]

***N*-(4-Methoxyphenyl)-4-nitrobenzenesulfonamide (3z).** (Equation 1). Following the general procedure, a mixture of 4-methoxyphenyl nonaflate (**1j**) (0.50 g, 1.23 mmol), 4-nitrobenzenesulfonamide (**2h**) (0.30 g, 1.48 mmol), K_3PO_4 (0.29 g, 1.35 mmol), $Pd_2(dba)_3$ (0.025 g, 28 μmol) and **III** (0.028 g, 66 μmol) in *t*-AmOH (4.2 mL) was stirred at 100 °C for 36 h. The crude product was purified via flash column chromatography (0−25% EtOAc/hexanes) to provide the title compound as a purple-white solid (0.32 g, 85%). ^{1}H NMR (400 MHz, DMSO) δ 10.23 (s, 1H), 8.43−8.32 (m, 2H), 7.97−7.88 (m, 2H), 7.04−6.95 (m, 2H), 6.89−6.79 (m, 2H), 3.69 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 156.3 (C), 149.1 (C), 144.3 (C), 128.6 (C), 127.8 (CH), 124.0 (CH), 123.6 (CH), 114.0 (CH), 55.0 (CH_3). HRMS (*m*/*z*): $[M - H]^-$ calcd for $C_{13}H_{11}N_2O_5S_1$ 307.0394; found 307.0395. Mp 180−183 °C, lit. mp 187−189 °C.[66]

***N*-(3,4-Dihydronaphthalen-2-yl)-4-methylbenzenesulfonamide (6).** (Scheme 1). Following the general procedure, a mixture of 3,4-dihydronaphthalen-2-yl nonaflate (**1q**) (0.50 g, 1.16 mmol), 4-tolylsulfonamide (**2b**) (0.24 g, 1.39 mmol), K_3PO_4 (0.27 g, 1.28 mmol), $Pd_2(dba)_3$ (0.0064 g, 7.0 μmol), **III** (0.0071 g, 17 μmol) and 4-Å molecular sieves (0.5 g) in *t*-AmOH (4.0 mL) was stirred at 80 °C for 15 h. The crude product was purified via flash column chromatography (10−20% EtOAc/hexanes) to provide the title compound as a white solid (0.28 g, 81%).^{1}H NMR (400 MHz, DMSO) δ 9.77 (br s, 1H), 7.74−7.70 (m, 2H), 7.36 (dd, *J* = 8.5, 0.6, 2H), 7.00 (td, *J* = 7.1, 1.9 Hz, 1H), 6.98−6.95 (m, 1H), 6.92 (td, *J* = 7.0, 1.4 Hz, 1H), 6.84 (d, *J* = 7.4, 1H), 6.06 (s, 1H), 2.61 (t, *J* = 8.1 Hz, 2H), 2.32 (s, 3H), 2.22−2.17 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 142.8 (C), 136.3 (C), 135.7 (C), 133.5 (C), 131.6 (C), 129.2 (CH), 126.5 (CH), 126.4 (CH), 126.0 (CH), 125.0 (CH), 124.7 (CH), 107.7 (CH), 27.2 (CH_2), 26.1 (CH_2), 21.1 (CH_3). HRMS (*m*/*z*): $[M - H]^-$ calcd for $C_{17}H_{16}N_1O_2S_1$ 298.0907; found 298.0896. Mp 116.3−120.5 °C.

Comparison of Initial Rates of Reactions (Table 4). General Procedure. In a glovebox, a 40-mL reaction vial equipped with a magnetic stir bar and fitted with Teflon screwcap was charged with K_3PO_4 (0.408 g, 1.92 mmol), $Pd_2(dba)_3$ (5.9 mg, 6.4 μmol) and ligand **III** (6.5 mg, 14 μmol). *t*-AmOH (1.5 mL) was added, the vial was placed on a metal heating block, the temperature was raised to 80 °C, and the mixture was stirred for 30 min. The vial was removed from the heating block and was charged with **1a**/4-bromotoluene/4-chlorotoluene (1.28−0.128 mmol), **2a** (1.54−0.384 mmol) and a known weight of 1,3,5-tri-isopropylbenzene (internal standard) were charged to the vial. *t*-AmOH (2.9 mL) was added and the reaction vial was returned to the metal heating block at 80 °C. A 20 μL aliquot was withdrawn from the reaction mixture at the interval of 5 min. The aliquot was diluted with acetonitrile (1 mL) and was injected into a HPLC instrument. The amount (mmol) of product **3a** was determined. The concentration of **3a** (mM) was plotted against time.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra of aryl nonaflates and reaction products and kinetic plots corresponding to the rate constants reported in Table 4. This material is available free of charge via the Internet at http://pubs.acs.org.

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(17) We have found that aryl nonaflates can be cleanly prepared from the parent phenols using nonafluorobutanesulfonyl fluoride in acetonitrile in the presence of 325-mesh potassium carbonate as the stoichiometric base.
(18) See ref 13 for a detailed account of Pd-catalyzed couplings of aryl nonaflates with secondary sulfonamides.
(19) Qualitative comparison of rates of reaction showed that the reaction proceeded 1.5 times faster when K_3PO_4 was used as base compared to the reaction when K_2CO_3 was used as base.
(20) The product was not isolated and the reported yield is an approximate yield based on HPLC.
(21) The coupled product was formed in 6% yield after 16 h at 80 °C in the absence of palladium and ligand.
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(46) *t*-AmOH contained 0.072 wt % water and K_3PO_4 contained 3.25 wt % water, and thus, a total of 0.4 equiv of water was present with respect to the limiting reagent, aryl nonaflate, in the reaction. No product arising from the hydrolysis of *p*-methylphenyl nonaflate was observed when the reaction shown in Table 2, entry 1 was performed in the presence of 1 equiv of added water. The coupled product **3b** was obtained in 97% solution assay yield. Although the base, K_3PO_4, was stored in a glovebox, this base was wet (3.25 wt %). No effort was made to dry the base prior to use. As described above, our reaction conditions are tolerant towards hydrolysis. Thus, we do not believe that strictly anhydrous K_3PO_4 is required for this reaction.
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