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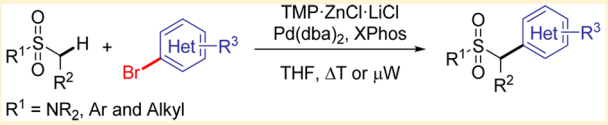
Palladium Catalyzed Monoselective α-Arylation of Sulfones and Sulfonamides with 2,2,6,6-Tetramethylpiperidine·ZnCl·LiCl Base and Aryl Bromides

Thomas Knauber* and Joseph Tucker

Worldwide Medicinal Chemistry, Pfizer Worldwide Research and Development, Groton, Connecticut 06340, United States

Supporting Information

ABSTRACT: A palladium catalyzed Negishi-type α-arylation of sulfones and sulfonamides with a broad range of aryl bromides has been developed. The substrates are selectively metalated *in situ* with tmp·ZnCl·LiCl base (tmp: 2,2,6,6-tetramethylpiperidine) and cross-coupled in the presence of a catalyst system that is generated from $Pd(dba)_2$ and XPhos. Electron-deficient, electron-rich, and heterocyclic aryl bromides have been successfully cross-coupled, and sensitive functional groups are well tolerated. Simple aryl bromides are converted overnight at 60 °C in THF while heteroaryl bromides are efficiently coupled within 2 h at 130 °C in a microwave reactor. The desired monoarylated α-branched benzyl sulfones and sulfonamides were obtained in good yields, and overarylation was not detected. The procedure is ideal for late stage functionalization in parallel medicinal chemistry.



INTRODUCTION

Sulfones and sulfonamides are important structural motifs in biologically active compounds.[1] In one of our medicinal chemistry projects, we set out to explore the structure−activity relationships (SAR)[2] of a series of α-branched heterocyclic benzyl sulfone and sulfonamide motifs on a heteroaromatic core (Scheme 1).

We aimed for the structural diversification to be performed in one high-yielding late step with a diverse set of starting materials and for the method to be transferable to the parallel syntheses of compound libraries. Traditional methods including alkylations,[3] Cu-catalyzed arylations,[4] Chan−Lam type arylations,[5] and aminations with N-electrophiles rely on the use of sulfinate salts as key intermediates which often have to be custom-made following alkylation[6] or oxidation[7] procedures. Initially, we accessed our target molecules by following the traditional sequence depicted in Scheme 1. Heterocyclic benzyl alcohols were transferred into the corresponding sodium sulfinates by an Appel reaction, alkylation with sodium 1-methyl 3-sulfinopropanoate (SMOPS), and elimination with sodium methoxide.[6] The sulfinate was reacted with hydroxylamine-*O*-sulfonic acid,[6] and the corresponding sulfonamide was coupled with the heteroaromatic core.[8] As a consequence, the overall yields are relatively low, and the processes are too step-intensive for library syntheses and thus did not meet our initial requirements. In particular, the synthesis of α-branched heterocyclic benzyl sulfonamides proved to be challenging, as the corresponding sulfonyl chlorides readily decompose into the corresponding benzyl chlorides with extrusion of sulfur dioxide (Scheme 2).[9] We observed decomposition of substrate **1** upon activation with thionyl chloride followed by an oxidative rearrangement.[10] The corresponding unsaturated side product **3** was obtained exclusively (Scheme 2).[9] In addition, free α-branched benzyl sulfonic acids are sensitive and gradually decompose upon storage.[11] Activations for the reaction with amines by the use of milder leaving groups such as electron-deficient phenolates[12] or *in situ* activation with $Ph_3PO/(TfO)_2$[13] also failed, and rearrangement to the corresponding olefinic sulfonamide was observed.

Significant research by the Willis group[14] and others[15] introduced sulfur dioxide adduct reagents for the synthesis of sulfones and sulfonamides, but general applicable syntheses of α-branched heterocyclic derivatives in compound libraries are still scarce.

Palladium-catalyzed α-arylations of easily accessible sulfones and sulfonamides caught our interest upon reviewing the chemical literature.[16] In general, the α-arylations (Scheme 3) start with deprotonation of the sulfone or sulfonamide substrate by a strong base (pK_a = 29 in DMSO for methyl phenyl sulfone).[17] The *in situ* generated *C*-nucleophile coordinates to a Pd^{II}−aryl complex, formed by oxidative addition of a Pd^0-complex to an aryl halide. Reductive elimination liberates the desired product and closes the catalytic cycle.

The method was pioneered by the group of Beletskaya in 2002.[16a] Subsequently, the groups of Koning[16b] and Oshima[16d] focused on the coupling of sulfones while the group of Northrup[16c] reported on the arylation of activated sulfamoyl acetates with subsequent multistep diversification of the coupling products. The group of Walsh developed an efficient arylation of alkyl aryl sulfones in the presence of $Pd(OAc)_2$ and the *N*-(dicyclohexylphosphino)-2-(2′-tolyl)-indole ligand.[16g,h] This phosphine is commercially available, but we observed slow oxidation and hydrolysis of the labile P−N bond over time. Consequently, we stepped back from pursuing this procedure. A $Pd(OAc)_2$/XPhos catalyzed arylation of phenyl methyl

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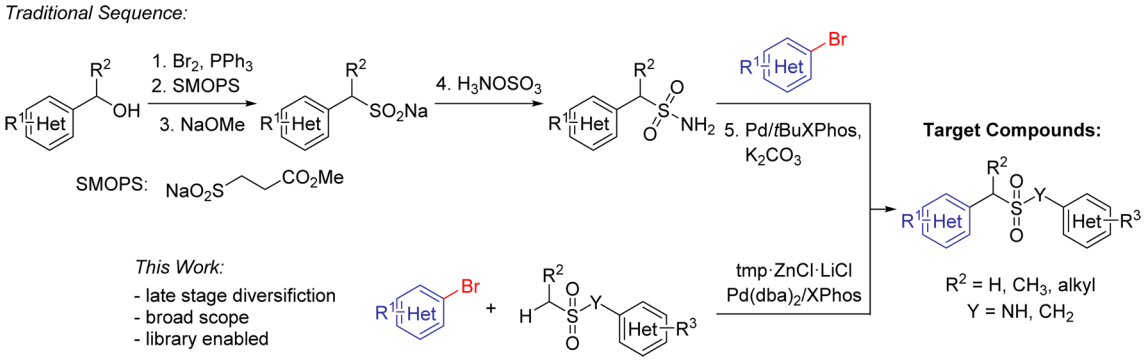
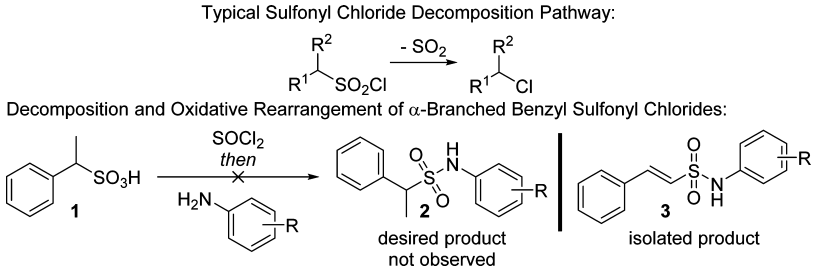
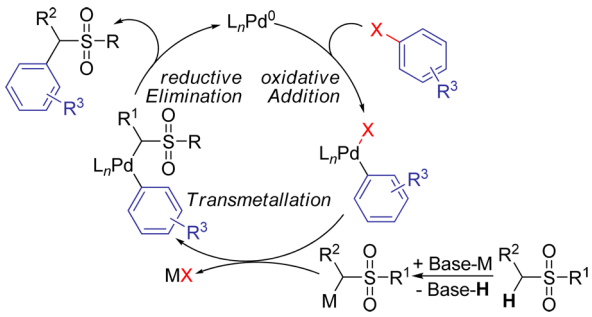
Scheme 1. Synthetic Strategies to α-Branched Heterocyclic Benzyl Sulfones and Sulfonamides



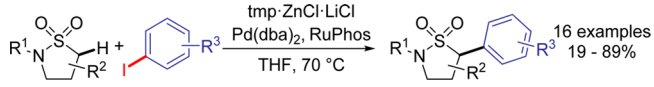
Scheme 2. Decomposition of Aliphatic Sulfonyl Chlorides



Scheme 3. Mechanistic Concept



Scheme 4. Selective α-Arylation of Sultams



sulfone was developed by Nambo and Crudden as the first step in their modular synthesis of triarylmethanes.[16i] Overarylation was successful minimized to less than 1% by using 3 equiv of the sulfone, LiO*t*Bu base, and cyclopentyl methyl ether as solvent. Zhou and co-workers reported the first method applicable to the arylation of both sulfones and sulfonamides.[16e,f] The method exhibits a broad scope, but overarylation was reported in some cases. The substrates are deprotonated, converted into the corresponding Negishi reagents at cryogenic temperatures, and subsequently cross-coupled with aryl halides. Overall, the procedure did not fully meet our requirements for applications in parallel medicinal chemistry, and we finally stopped pursuing this method after we were unable to reproduce the reaction with our target compounds. Recently, René and colleagues developed the α-arylation of cyclic sulfonamides (sultams) with aryl iodides in the presence of a Pd/RuPhos catalyst and Knochel's tmp·ZnCl·LiCl[18] base (tmp: 2,2,6,6-tetramethylpiperidine) (Scheme 4) which gave high selectivity for the monoarylated products.[19]

Unfortunately for our purpose, the group focused their study exclusively on sultams and aryl iodides as starting materials. However, they demonstrated that the use of tmp·ZnCl·LiCl could afford a competent organozinc species to engage in Negishi coupling chemistry by an operationally simple means without requiring prolonged deprotonation and salt metathesis steps at cryogenic temperatures, which substantially increase the operational difficulty when applied to parallel synthesis.

With this in mind, we envisaged that a general Pd-catalyzed Negishi-type α-arylation procedure would enable the late stage diversification of acyclic α-branched sulfones and sulfonamides. The use of tmp·ZnCl·LiCl promises high monoselectivity for the arylation, relative to previous methods, and would allow a method suited for compound library syntheses in parallel. We also aimed to broaden the scope to aryl and heteroaryl bromides which are available in considerably broader structural diversity than aryl iodides.

RESULTS AND DISCUSSION

We chose phenyl methyl sulfone (**4a**) and 4-bromotoluene (**5a**) as model substrates, which were reacted in the presence of tmp·ZnCl·LiCl and $Pd(dba)_2$ in anhydrous THF at 60 °C (Table 1). The base is commercially available or can be prepared following the literature procedures.[20] The desired cross-coupling product **6aa** was not detected with triphenylphosphine (Table 1, entry 1), with tri(2-furyl)phosphine (Table 1, entry 2), or in the absence of a ligand. Further experiments demonstrated that bulky, electron-rich, monodentate phosphines (Table 1, entries 1–6) are competent ligands for the arylation. The use of DavePhos (Table 1, entry 3) and RuPhos (Table 1, entry 4), which is highly efficient in René's procedure,[19] resulted in moderate conversion of a 38% and 45% yield, respectively. Full conversion of the starting materials was detected with XPhos (Table 1, entry 5) and BrettPhos (Table 1, entry 6).[21] We decided to carry on with the

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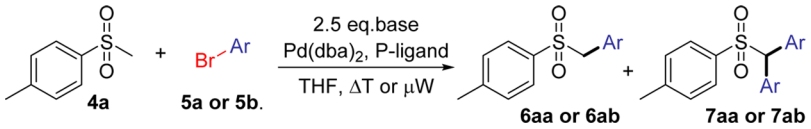
Table 1. Optimization of the Reaction Conditions[a]



	Ar	P-ligand [mol %]	Base	T [°C]	t [h]	**6** [%][a]	**7** [%][a]
1	4-Tol	PPh_3 (2)	tmp·ZnCl·LiCl	60	16	0	0
2	4-Tol	P(2-furyl)$_3$ (2)	tmp·ZnCl·LiCl	60	16	0	0
3	4-Tol	DavePhos (2)	tmp·ZnCl·LiCl	60	16	38	0
4	4-Tol	RuPhos (2)	tmp·ZnCl·LiCl	60	16	45	0
5[a]	**4-Tol**	**XPhos (2)**	**tmp·ZnCl·LiCl**	**60**	**16**	**99 (isol.)**	**0**
6	4-Tol	BrettPhos (2)	tmp·ZnCl·LiCl	60	16	99	0
7	4-Tol	Xantphos (2)	tmp·ZnCl·LiCl	60	16	36	0
8	4-Tol	rac. BINAP (2)	tmp·ZnCl·LiCl	60	16	0	0
9	4-Tol	XPhos (2)	LiO*t*Bu	60	16	0	0
10[b]	4-Tol	XPhos (10)	LiO*t*Bu	60	16	26	10
11[b]	4-Tol	XPhos (10)	NaO*t*Bu	60	16	11	3
12[b]	4-Tol	XPhos (10)	KO*t*Bu	60	16	0	0
13[b]	4-Tol	XPhos (10)	LiHMDS	60	16	0	0
14[b]	4-Tol	XPhos (10)	LiO*t*Bu	120	16	29	12
15	3-Py	XPhos (2)	tmp·ZnCl·LiCl	60	16	traces	0
16	3-Py	XPhos (2)	tmp·ZnCl·LiCl	60	96	traces	0
17	3-Py	XPhos (2)	tmp·ZnCl·LiCl	80	16	55	0
18	3-Py	XPhos (2)	tmp·ZnCl·LiCl	130 (μW)	2	24	0
19	3-Py	**XPhos (10)**	tmp·ZnCl·LiCl	**130 (μW)**	**2**	**72 (isol.)**	0
20	3-Py	XPhos (10)	tmp·ZnCl·LiCl	150 (μW)	1	34	0

[a]Methyl-(4-tolyl)-sulfone (**4a**) (0.25 mmol, 1.0 equiv), 4-bromotoluene (**5a**) (0.275 mmol, 1.1 equiv) or 3-bromopyridine (**5b**) (0.275 mmol, 1.1 equiv), base (0.625 mmol, 2.5 equiv), $Pd(dba)_2$ (equimolar to the ligand), phosphine ligand, anhydrous THF (0.07 M). Yields were determined by ^{1}H NMR with mesitylene as internal standard unless noted otherwise. [b]Anhydrous 1,4-dioxane (0.07 M) was used as solvent. DavePhos: 2-dicyclohexylphosphino-2′-(*N*,*N*-dimethylamino)biphenyl. RuPhos: 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl. XPhos: 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl. BrettPhos: 2-(dicyclohexylphosphino)-3,6-dimethoxy-2′,4′,6′-triisopropyl-1,1′-biphenyl. Xanthphos: 4,5-bis(diphenylphosphino)-9,9-dimethyl-xanthene. BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene.

somewhat cheaper and more common XPhos ligand. The addition of bidentate ligands such as Xantphos (Table 1, entry 7) and racemic BINAP (Table 1, entry 8) reduced the yield of the desired coupling product to 36% and 0%, respectively.

As anticipated, the reactions were highly monoselective and the overarylated side product **7aa** was not detected (Table 1 entries 1−8). Having identified an ideal procedure for the coupling of the model substrates we set out to benchmark the conditions against more commonly used bases, and we chose lithium, sodium, and potassium *tert*-butylate as well as lithium hexamethyldisilazane which have been successfully employed earlier.[16] However, the desired product **6aa** was not detected with these bases in tetrahydrofuran (Table 1, entry 9) even with 10 mol % of the catalyst system. Low quantities of **6aa** along with diarylated side product **7aa** were obtained in 1,4-dioxane (Table 1, entries 10 and 11) with LiO*t*Bu giving the best result of 26% of the desired product **6aa** along with 10% of the side product **7aa** (Table 1, entry 10). Sodium *tert*-butylate gave product **6aa** in 11% yield along with 3% side product (Table 1, entry 11), while no conversion was observed with potassium *tert*-butylate (Table 1, entry 12) and the use of LiHMDS resulted in decomposition of the substrates (Table 1, entry 13). A slight step-up in yield was observed at 120 °C with LiO*t*Bu which produced 20% of **6aa** along with 12% of the undesired side product **7aa** (Table 1, entry 14). These results clearly demonstrate the synthetic benefits of using the more elaborate tmp·ZnCl·LiCl over commonly used bases which allows relatively mild reaction conditions and excellent monoselectivity.

Encouraged, we turned our attention to the pharmaceutically relevant coupling of nitrogen containing heteroaryl bromides which are often challenging to convert because of coordination of the nitrogen atom to the palladium catalyst.[22] We chose 3-bromopyridine (**5b**) as a model substrate, which gave traces of the desired coupling product **6ab** under the previously optimized reaction conditions (Table 1, entry 15).

Extending the reaction time to 96 h did not improve the yield (Table 1, entry 16). However, a boost in yield (55%) was obtained by heating the reaction mixture in a sealed vial at 80 °C (Table 1, entry 17). We opted to conduct the coupling reactions in a microwave reactor which offers safer heating and emergency shut-off prevents dangerous overpressurization of the vessel. In our first microwave experiment, the desired product was detected in 24% yield after 2 h of irradiation at 130 °C (Table 1, entry 18). The starting materials were recovered, and we hypothesized that the active palladium catalyst might have decomposed prematurely. Increasing the $Pd(dba)_2$/XPhos loading to 10 mol % resulted in the isolation of the desired product in 72% yield (Table 1, entry 19). Further increasing the reaction temperatures resulted in significant decomposition, and the desired product was detected in only 34% at 150 °C along with undefined side products (Table 1, entry 20).

With the optimized procedures, using both conventional and microwave heating, in hand, we set out to investigate the scope of the α-arylation of sulfones with aryl bromides (Scheme 5). In general, higher yields were obtained with the microwave protocol in comparison to the thermal procedure. Electron-rich (**5c** and **5d**), electron-deficient (**5i**, **5j**, and **5k**), and sterically

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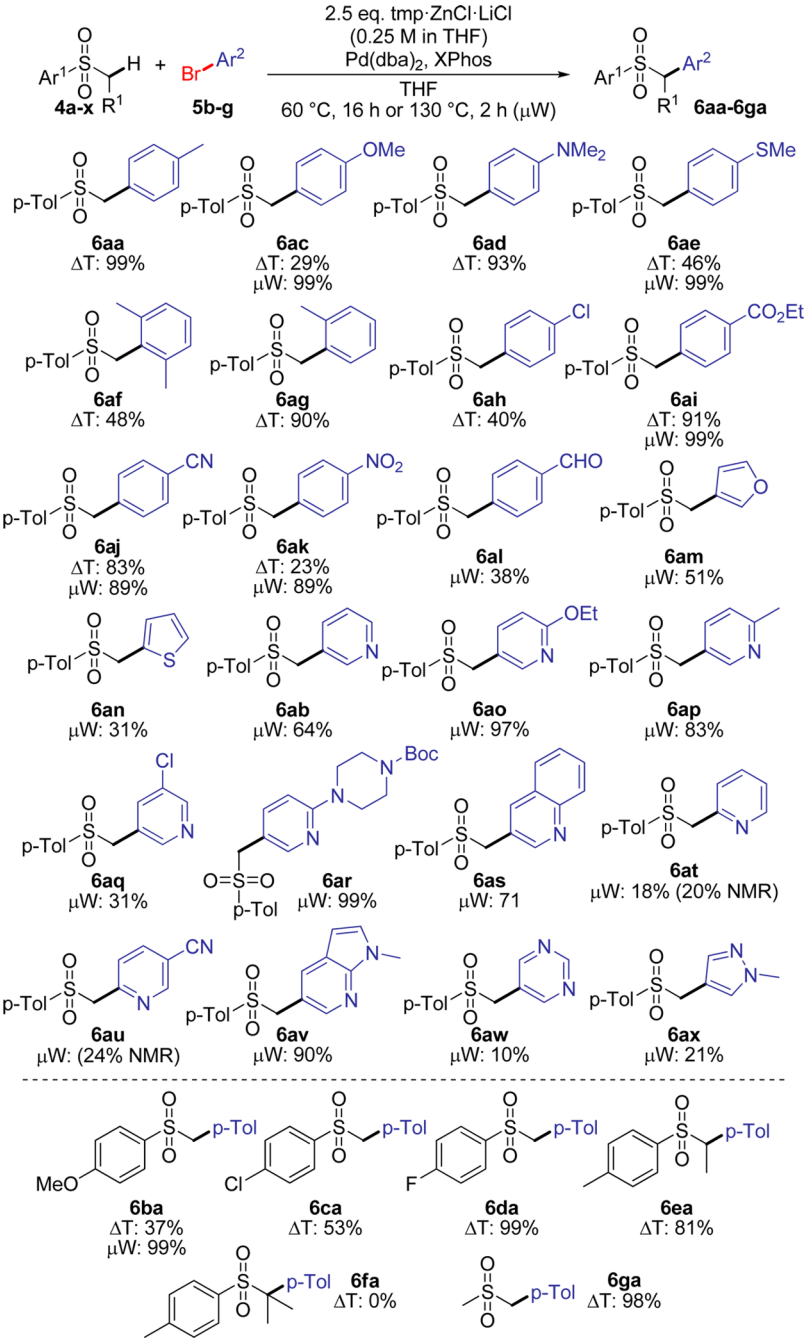
Scheme 5. Coupling of Sulfones with Aryl Bromides[a]



[a]Sulfone (0.5 mmol, 1.0 equiv), aryl bromide (0.55 mmol, 1.1 equiv), tmp·ZnCl·LiCl-solution (0.25 M in THF, 5 mL, 2.5 equiv) (tmp: 2,2,6,6-tetramethylpiperidine), anhydrous tetrahydrofuran (2 mL). Thermal heating: $Pd(dba)_2$ (2 mol %), XPhos (2 mol %), 60 °C, 16 h. Microwave protocol: $Pd(dba)_2$ (10 mol %), XPhos (10 mol %), 130 °C, 2 h. Yields in parentheses are determined by ^1H NMR with mesitylene as internal standard. XPhos: 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

demanding aryl bromides (**5f** and **5g**) were smoothly converted to give the desired monocoupled products (**6**). Furthermore, functional groups such as ester (**5i**), nitrile (**5j**), nitro (**5k**), and even formyl (**5l**) groups were well tolerated.

1-Bromo-4-chlorobenzene (**5h**) was selectively functionalized at the C−Br bond which leaves the C−Cl bond as an anchor for further functionalization. The result also excludes aryl chlorides as substrates. A broad range of pharmaceutically relevant heterocyclic aryl bromides (**5m**−**5x**) was successfully cross-coupled with the optimized procedure. High yields were obtained for most 3-bromopyridines (**5b** and **5o**−**5s**) or azaindoles (**5v**). The five-membered heterocycles 3-bromofurane (**5m**) and 2-bromothiophene (**5n**) were converted in moderate yields of 51% and 31% respectively. We were pleased that even highly challenging but pharmaceutically impactful heterocycles were successfully converted albeit in lower yields. However, the method provides broad structural diversity in compound libraries which is crucial for the elucidation of structure−activity relationships within the drug discovery process. 2-Bromopyridines (**5t** and **5u**) were converted, and

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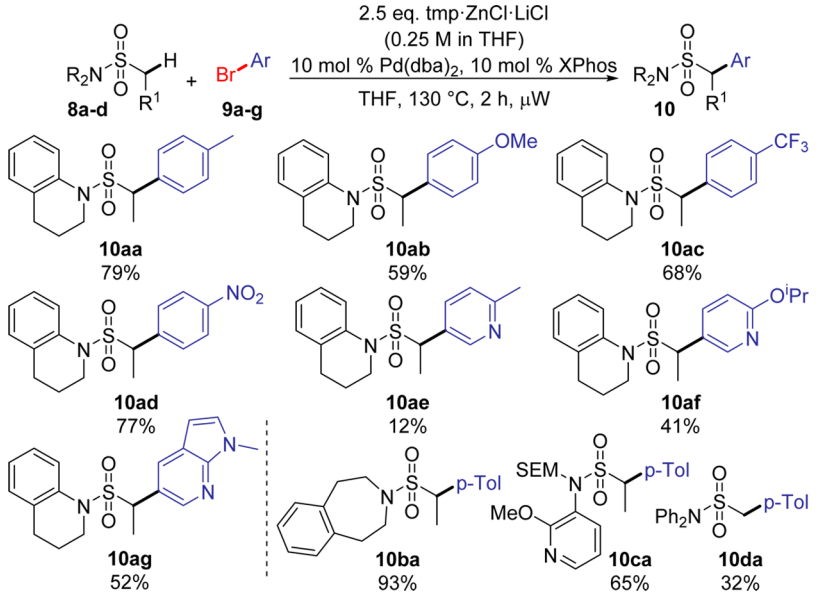
Scheme 6. α-Arylation of Sulfonamides[a]



[a]Sulfonamide (0.5 mmol, 1.0 equiv), aryl bromide (0.55 mmol, 1.1 equiv), $Pd(dba)_2$ (10 mol %), XPhos (10 mol %), tmp·ZnCl·LiCl-solution (0.25 M in THF, 5 mL, 2.5 equiv) (tmp: 2,2,6,6-tetramethylpiperidine), anhydrous tetrahydrofuran (2 mL), 130 °C in microwave reactor, 2 h. XPhos: 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

the corresponding products **6at** and **6au** were obtained in 18% and 24%. 5-Bromopyrimidine (**5w**) yielded the desired product **6aw** in 10% yield, and even 4-bromo-*N*-methylpyrazole (**5x**) gave the corresponding product in 21% yield.

We then turned our attention to the sulfone coupling partners. Electron-rich (**4b**) and electron-deficient (**4d**) aryl methyl sulfones were successfully coupled with 4-bromotoluene (**4a**). Dimethyl sulfone (**4g**) was exclusively monoarylated, and the product **6ga** was isolated in near quantitative yield. Furthermore, tolyl ethyl sulfone (**4e**) was coupled in 81% yield. Products that could arise from β-hydride elimination were not detected, and the crude reaction mixture consisted of the desired product and traces of both substrates. Increasing the steric bulk on the sulfone shut down the cross-coupling completely, and *p*-tolyl isopropyl sulfone (**4f**) was fully recovered. We hypothesize that this steric sensitivity is likely the reason for the high monoselectivity of the process, and the corresponding monoarylated products were obtained exclusively for all tested substrates.

Having established an efficient procedure for the α-functionalization of sulfones, we continued our investigation with the arylation of sulfonamides (Scheme 6). The substrates (**8a−8d**) were prepared by sulfonylation of the corresponding amines with inexpensive methanesulfonyl chloride or ethanesulfonyl chloride. The sulfonamides (**8a−d**) were successfully cross-coupled with a set of aryl bromides (**9a−g**). These results illustrate our alternate synthetic strategy to access α-branched benzylic sulfonamides which circumvents the chemical instability observed with the corresponding sulfonyl chlorides. The cross-couplings were performed in a microwave reactor, and the desired α-branched products (**10**) were obtained in good yields. Electron-rich (**9b**), electron deficient (**9c−d**), and heterocyclic aryl bromides (**9e−g**) were smoothly converted, and the reaction has a similar scope to the arylation of sulfones (Scheme 5). Finally, we turned our attention to the sulfonamide coupling partner. The amides of aliphatic (**8a** and **8b**) and aromatic amines (**8c** and **8d**) were successfully reacted with 4-bromotoluene (**9a**). The N−H bond of **8c** was protected with an SEM group to prevent deprotonation by tmp·ZnCl·LiCl, and product **10ca** was obtained in 65% yield. Product **10da** was isolated in moderate 32% yield, but no side products were detected in the reaction mixture.

CONCLUSION

A Pd/XPhos-catalyzed Negishi-type α-arylation of easily accessible acyclic sulfones and sulfonamides with aryl bromides in the presence of tmp·ZnCl·LiCl has been developed. The arylation reaction has a broad scope, and the desired α-branched products have been obtained in good yields and excellent monoselectivities. This procedure marks an effective strategy to access α-substitued benzylic sulfonamides, for which the corresponding sulfonyl chlorides are unstable. The operationally simple procedure is ideal for the execution of compound libraries and enabled us to explore structure−activity relationships rapidly which were otherwise inaccessible in ongoing drug discovery projects.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all reagents were obtained from commercial suppliers and used without further purification. Anhydrous solvents were purchased from Acros (AcroSeal) or EMD Chemicals (DriSolv) and used as received. Zinc chloride solution (0.5 M) in tetrahydrofuran, *p*-tolyl sulfinate, and *n*-butyl lithium solution (2.5 M in hexanes) were purchased from Aldrich and used as received. 2,2,6,6-Tetramethylpiperidinylzinc chloride lithium chloride complex (tmp·ZnCl·LiCl) is commercially available from Rockwood Lithium Inc. or can be prepared following the literature-known procedures.[18] Reactions were performed in regular glassware under a nitrogen atmosphere. Solid materials were added under air, and the reaction vessel was closed, evacuated for 5 min, and refilled with dry nitrogen (3 purge cycles). Analytical thin-layer chromatography was performed with precoated silica gel 60 F254 glass plates with a 250 μm layer thickness. The spots were visualized under UV irradiation (λ = 254 nM) and $KMnO_4$ stains. Reactions under microwave irradiation were performed in a Biotage Initiator microwave

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reactor using designated glassware and crimp-top septa. The temperature was measured with an IR-sensor on the outside of the reaction vial. Isolations and purifications were accomplished by medium performance liquid chromatography (MPLC) with heptane and ethyl acetate eluents and prepacked silica gel cartridges (12 g silica and 24 g silica). Proton (^{1}H NMR), fluorine (^{19}F NMR), and carbon (^{13}C{1H}NMR) nuclear magnetic spectroscopy data were recorded on 300 or 400 MHz spectrometers. Carbon spectra are proton decoupled. Chemical shifts are reported in ppm (δ) and referenced to the deuterated solvent residual peak. The obtained data are reported with s = singlet, d = doublet, t = triplet, q = quartet, m = multiple and br = broad signal. Coupling constants are given in Hz. GC-MS data were acquired with scanning from 50 to 550 Da. An HP-1 column (12 m × 0.2 mm × 0.33 μm) with helium carrier gas was used. Samples for high resolution mass spectrometry (HRMS) were separated on a UPLC system and analyzed by TOF mass spectrometery in positive electrospray mode. The recorded spectra were automatically lockmass corrected, and the mass accuracy for all observed isotopes was calculated against the theoretical ion mass derived from the chemical formula. IR spectra of neat liquid and solid samples were recorded on an FTIR spectrometer with a diamond ATR scanning from 4000 to 500 nm. Frequencies are reported in cm^{-1}.

General Procedure for the Negishi Arylation of Sulfones and Sulfonamides (Method A). The corresponding sulfone or sulfonamide (1.00 equiv), the aryl bromide (1.10 equiv, if solid), bis(dibenzylideneacetone)palladium (2.00 mol %), and 2-dicyclohexylphosphino-2′,4′,6′-triiso-propylbiphenyl (XPhos, 2.0 mol %) were weighed in a reaction vial, capped, evacuated, and refilled with nitrogen (3 purge cycles, 5 min each). Anhydrous tetrahydrofuran (4 mL/mmol) and the aryl bromide (1.10 equiv, if liquid) were added, and the resulting dark solution was stirred for 10 min at room temperature. A solution of 2,2,6,6-tetramethylpiperidinylzinc chloride lithium chloride complex (tmp·ZnCl·LiCl, 0.25 M in tetrahydrofuran, 2.50 equiv) was added, and the resulting bright orange-brown solution was heated at 60 °C for 16 h. After cooling to room temperature, the brown reaction mixture was quenched with diluted sodium bicarbonate solution and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine, dried with sodium sulfate, filtered, and concentrated. The remaining crude mixture purified by column chromatography (silica gel, heptane/ethyl acetate gradient).

General Procedure for the Negishi Arylation under Microwave Irradiation (Method B). The corresponding sulfone or sulfonamide (1.00 equiv), the aryl bromide (1.2 equiv, if solid), bis(dibenzylideneacetone)palladium (10.0 mol %), and 2-dicyclohexylphosphino-2′,4′,6′-triiso-propylbiphenyl (XPhos, 10.0 mol %) were weighed in a microwave reaction vial, capped, evacuated, and refilled with nitrogen (3 purge cyles, 5 min each). Anhydrous tetrahydrofuran (4 mL/mmol) and the aryl bromide (1.20 equiv, if liquid) were added, and the resulting dark solution was stirred for 10 min at room temperature. A solution 2,2,6,6-tetramethylpiperdinylzinc chloride lithium chloride complex (tmp·ZnCl·LiCl, 0.25 M in tetrahydrofuran, 2.50 equiv) was added, and the crimp cap was replaced under a stream of nitrogen. The bright orange-brown reaction mixture was placed in the microwave reactor, prestirred for 5 s, and heated at 130 °C for 2 h. After cooling to room temperature, the brown reaction mixture was quenched with diluted sodium bicarbonate solution and extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were washed with brine, dried with sodium sulfate, filtered, and concentrated. The remaining crude mixture was purified by column chromatography (silica gel, heptane/ethyl acetate gradient).

Preparation of Starting Materials. *5-Bromo-N-methyl-7-azaindole (**5v** and **9g**) [CAS: 183208-22-2].* 5-Bromo-7-azaindole (1.00 g, 5.08 mmol) and sodium hydride (60% dispersion in mineral oil, 244 mg, 5.58 mmol) were weighed in a 100 mL round-bottom flask with septa, evacuated, and refilled with nitrogen (3 purge cycles). The mixture was suspended in anhydrous tetrahydrofuran and stirred at room temperature for 2 h. Iodomethane (792 mg, 5.58 mmol, 348 μL) was added, and the resulting mixture was stirred for 16 h at room temperature. The reaction mixture was quenched with methanol (2 mL) and concentrated. The remaining residue was dissolved in ethyl acetate (30 mL) and washed with saturated aqueous sodium bicarbonate solution (20 mL).The aqueous layer was re-extracted with ethyl acetate (2 × 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, filtered, and concentrated. The remaining crude was purified by flash chromatography (silica gel, *n*-heptane/ethyl acetate gradient). The desired product (898 mg, 4.25 mmol, 84%) was obtained as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.88 (s, 3 H), 6.40 (d, J = 3.51 Hz, 1 H), 7.19 (d, J = 3.51 Hz, 1 H), 8.02 (d, J = 2.34 Hz, 1 H), 8.35 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 31.4, 98.9, 111.5, 122.0, 130.4, 130. 7, 143.3, 146.2 ppm; MS (EI): m/z (%) = 211 [M]$^+$ (100), 184 (5), 157 (2), 130 (35), 103 (20), 84 (15); IR: υ = 2920 (w), 1512 (s), 1469 (s), 1399 (s), 1344 (m), 1268 (s), 1238 (w), 1125 (w), 1075 (m), 880 (m), 719 (s) cm^{-1}. The obtained data match those reported in the literature.[23]

*p-Tolyl Ethyl Sulfone (**4e**) [CAS: 7569-34-8].* The sodium tolyl sulfinate (649 mg, 4.00 mmol) was dissolved in dimethyl sulfoxide (5 mL), and ethyl iodide (936 mg, 6.00 mmol, 482 μL) was added. The colorless suspension was stirred at room temperature over the weekend. The reaction mixture was diluted ethyl acetate (30 mL) and washed with saturated aqueous sodium bicarbonate solution (50 mL). The aqueous layer was re-extracted with ethyl acetate (2 × 20 mL). The combined organic layers were washed with brine, dried with sodium sulfate, filtered, and concentrated. The brown crude was purified by column chromatography, and *p*-tolyl ethyl sulfone (**4e**) (274 mg, 1.49 mmol, 37%) was obtained as a colorless solid after recrystallization from ethyl acetate/heptane. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.27 (t, J = 7.41 Hz, 3 H), 2.46 (s, 3 H), 3.10 (q, J = 7.41 Hz, 2 H), 7.37 (d, J = 8.20 Hz, 2 H), 7.73−7.83 (m, 2 H); ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 7.5, 21.6, 50.6, 128.2, 129.8, 135.6, 144.6 ppm, MS (EI): m/z (%) = 184 [M]$^+$ (50), 155 (55), 139 (20), 91 (100), 65 (40); IR: υ = 2923 (w), 1591 (m), 1453 (w), 1406 (w), 1313 (m), 1294 (m), 1142 (s), 1084 (m), 813 (m), 775 (m), 728 (s) cm^{-1}. The obtained data match those reported in the literature.[24]

*1-(Ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (**8a**) [CAS: 544456-91-9].*[25] A 500 mL three necked flask equipped with a reflux condenser was evacuated and refilled with nitrogen (3 purge cycles). Anhydrous chloroform (200 mL), 1,2,3,4-tetrahydroquinoline (9.99 g, 75.9 mmol, 9.40 mL), and anhydrous pyridine (7.91 g, 100 mmol, 8.00 mL) were added. The mixture was cooled to 0 °C, and ethyl sulfonyl chloride (6.43 g, 50.0 mmol, 4.72 mL) was added dropwise within 30 min. After complete addition, the reaction mixture was heated to reflux for 4 h. The reaction mixture was cooled to room temperature and washed with ammonium hydroxide solution (12%, 150 mL). The aqueous layer was re-extracted with dichloromethane (2 × 100 mL). The combined organic layers were washed with brine (50 mL), dried with sodium sulfate, filtered, and concentrated. The crude orange oil was purified by flash column chromatography (silica gel, *n*-heptane/ethyl acetate gradient). A brownish oil was obtained that was further purified by distillation under reduced pressure (heating block: 180 °C, bp: 145 °C). The desired product was obtained as a light yellow oil (8.52 g, 37.8 mmol, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.34 (t, J = 7.41 Hz, 3 H), 1.95−2.06 (m, 2 H), 2.85 (t, J = 6.63 Hz, 2 H), 3.12 (q, J = 7.41 Hz, 2 H), 3.76−3.84 (m, 2 H), 6.98−7.07 (m, 1 H), 7.08−7.18 (m, 2 H), 7.64 (dd, J = 8.39 Hz, J = 0.98 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 7.9, 22.6, 27.0, 46.3, 46.4, 121.8, 123.9, 126.6, 128.6, 129.6, 137.0 ppm; MS (EI): m/z (%) = 225 [M]$^+$ (40), 181 (1), 160 (1), 132 (100), 105 (10), 77 (10); IR: υ = 2940 (w), 1488 (m), 1453 (m), 1331 (s), 1253 (m), 1143 (s), 1086 (m), 1041 (m), 973 (m), 846 (m), 754 (s) cm^{-1}. The obtained data match those reported in the literature for 1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoline.[26]

*3-(Ethylsulfonyl)-2,3,4,5-tetrahydrobenzoazepine (**8b**) [CAS: 1484866-61-6].* A 50 mL round-bottom flask was charged with 2,3,4,5-tetrahydrobenzoazepinium hydrochloride. Dichloromethane (25 mL) and trimethylamine (1.13 g, 11.2 mmol, 1.56 mL) were added. The mixture was stirred until a clear homogeneous solution was obtained. Ethyl sulfonyl chloride (1.43 g, 11.2 mmol, 1.06 mL) was added dropwise, and the mixture was stirred for 15 min at room temperature. The reaction mixture was washed with water (100 mL),

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and the aqueous layer was re-extracted with dichloromethane (20 mL). The combined organic layers were dried with sodium sulfate, filtered, and concentrated. The remaining brownish oil was purified by flah column chromatography (silica gel, *n*-heptane/ethyl acetate gradient). The desired product was obtained as a colorless solid (240 mg, 1.00 mmol, 27%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.32 (t, J = 7.41 Hz, 3 H), 2.95 (q, J = 7.41 Hz, 2 H), 2.98−3.04 (m, 4 H), 3.41−3.52 (m, 4 H), 7.09−7.19 (m, 4 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 7.7, 38.1, 45.2, 48.0, 126.5, 129.3, 140.3 ppm; MS (EI): m/z (%) = 239 $[M]^+$ (50), 213 (1), 194 (1), 146 (100), 117 (75), 91 (25); IR: υ = 2903 (w), 1497 (w), 1451 (w), 1321 (s), 1281 (m), 1133 (s), 1081 (s), 1032 (m), 937 (m), 895 (s), 771 (s), 737 (s) cm^{-1}.

N-(2-Methoxypyridin-3-yl)ethanesulfonamide [CAS: 1341535-24-7]. A 20 mL screw cap vial with PTFE septa was charged with 3-amino-2-methoxy pyridine (621 mg, 5.00 mmol), evacuated, and refilled with nitrogen (3 purge cycles). Anhydrous dichloromethane (5 mL), triethylamine (759 mg, 7.50 mmol, 1.05 mL), and ethane sulfonyl chloride (707 mg, 5.50 mmol, 520 μL) were added. The reaction mixture was stirred 16 h at room temperature. The reaction mixture was diluted with dichloromethane (20 mL) and washed with saturated sodium bicarbonate solution (50 mL). The aqueous layer was re-extracted with dichloromethane (2 × 20 mL). The combined organic layers were washed with brine (50 mL), dried with sodium sulfate, filtered, and concentrated. The crude product was concentrated and purified by flash chromatography (silica gel, *n*-heptane/ethyl acetate gradient). The desired product was obtained as a light yellow oil (710 mg, 3.28 mmol, 66%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (t, J = 7.43 Hz, 3 H), 3.04−3.13 (m, 2 H), 4.01 (s, 3 H), 6.72 (s_{br}, 1 H), 6.90 (dd, J = 7.73 Hz, J = 4.99 Hz, 1 H), 7.78 (dd, J = 7.73 Hz, J = 1.66 Hz, 1 H), 7.88−7.96 (m, 1 H) ppm; ^{13}C{1H}NMR (101 MHz, $CDCl_3$) δ = 8.1, 46.1, 53.9, 117.4, 121.4, 127.0, 141.8, 154.0 ppm; MS (EI): m/z (%) = 216 $[M]^+$ (65), 187 (2), 151 (2), 123 (99), 93 (100), 72 (20); IR: υ = 3075 (br., w), 2929 (w), 1596 (m), 1476 (s), 1437 (s), 1408 (s), 1323 (s), 1196 (m), 1141 (s), 1109 (s), 1009 (m), 922 (m), 851 (m), 763 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_8H_{12}N_2NaO_3S$: 239.0458; found: 239.0461. The obtained data match those reported in the literature for *N*-(2-methoxypyridin-3-yl)methanesulfonamide.[27]

*N-(2-Methoxypyridin-3-yl)-N-((2-(trimethylsilyl)ethoxy)methyl)-ethanesulfonamide (**9c**).* Sodium hydride (60% in mineral oil, 128 mg, 3.19 mmol) and *N*-(2-methoxypyridin-3-yl)-ethanesulfonamide (575 mg, 2.66 mmol) were weighed in a 25 mL round-bottom flask, evacuated, and refilled with nitrogen (3 purge cycles). Anhydrous *N*,*N*-dimethylformamide (5 mL) was added, and the resulting mixture was stirred for 1 h at room temperature. 2-(Trimethylsilyl)ethoxymethyl chloride (493 mg, 2.66 mmol, 534 μL) was added, and the mixture was stirred for 30 min at room temperature. The reaction mixture was quenched with water and extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried with sodium sulfate, filtered, and concentrated. The remaining yellow oil was purified by flash chromatography (silica gel, *n*-heptane/ethyl acetate gradient). The title compound was obtained as a colorless oil (864 mg, 2.49 mmol, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = −0.02 (s, 9 H), 0.84−0.90 (m, 2 H), 1.35 (t, J = 7.41 Hz, 3 H), 3.01 (q, J = 7.28 Hz, 2 H), 3.64−3.71 (m, 2 H), 3.96 (s, 3 H), 4.99 (s, 2 H), 6.92 (dd, J = 7.61 Hz, J = 4.88 Hz, 1 H), 7.64 (dd, J = 7.61 Hz, J = 1.76 Hz, 1 H), 8.11−8.14 (m, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = −1.5, 7.7, 17.6, 47.7, 53.5, 65.1, 79.1, 117.3, 121.0, 142.2, 146.9, 159.8 ppm; MS (EI): m/z (%) = 346 $[M]^+$ (1), 317 (1), 288 (100), 259 (5), 229 (55), 180 (20), 136 (60), 107 (30), 73 (80); IR: υ = 2952 (w), 1469 (s), 1408 (s), 1339 (s), 1247 (m), 1215 (m), 1156 (s), 1078 (s), 1013 (s), 857 (s), 833 (s), 771 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{26}N_2NaO_4SSi$: 369.1278; found: 369.1275.

2,2,6,6-Tetramethylpiperidinylzinc Chloride Lithium Chloride Complex (tmp·ZnCl·LiCl) [CAS: 1145881-09-9].[18] A hot 100 mL round-bottom flask with a new rubber septa was evacuated and refilled with nitrogen (3 purge cycles). 2,2,6,6-Tetramethylpiperidine (1.13 g, 8.00 mmol, 1.36 mL) was added, dissolved in anhydrous tetrahydrofuran (4 mL), and cooled to −78 °C in an acetone/dry ice bath. A solution of *n*-butyl lithium in hexanes (2.6 M, 8.00 mmol, 3.20 mL) was added dropwise within 5 min. The resulting light yellow solution was stirred at the given temperature for an additional 5 min and was allowed to warm to room temperature. The solvent was removed *in vacuo*, and the resulting light yellow solid was dissolved in tetrahydrofuran (16 mL). (Note: 2,2,6,6-tetramethylpiperidinyl lithium turns into an orange gum when exposed to traces of air. The resulting material is only moderately soluble in tetrahydrofuran). A solution of zinc chloride in tetrahydrofuran (0.5 M, 8.00 mmol, 16 mL) was added. The reaction is slightly exothermal. The resulting light yellow solution (0.25 M) was used as received and is stable upon storage when kept under a protective atmosphere.

Preparation of the Cross-Coupling Products. *1-Methyl-4-(4-methylbenzylsulfonyl)benzene (**6aa**) [CAS: 21668-99-5].* The compound was prepared according to method A from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromotoluene (94.1 mg, 0.55 mmol), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (129.8 mg, 0.50 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 99% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.33 (s, 3 H), 2.43 (s, 3 H), 4.26 (s, 2 H), 6.95−7.01 (m, 2 H), 7.05−7.11 (m, 2 H), 7.25 (m, 2 H), 7.49−7.55 (m, 2H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.2, 21.6, 62.6, 125.1, 128.6, 129.2, 129.5, 130.7, 135.1, 138.6, 144.5 ppm; MS (EI): m/z (%) = 260 $[M]^+$ (5), 207 (1), 181 (3), 153 (1), 105 (100), 77 (10); IR: υ = 2923 (w), 1593 (w), 1415 (w), 1301 (s), 1286 (s), 1183 (s), 1143 (s), 1083 (m), 815 (s), 690 (s) cm^{-1}. The obtained data match those reported in the literature.[28]

*3-(Tosylmethyl)pyridine (**6ab**) [CAS 106651-91-6].* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 3-bromopyridine (94.8 mg, 0.60 mmol, 58 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (79.0 mg, 0.32 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 64% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.38 (s, 3 H), 4.27 (s, 2 H), 7.18−7.26 (m, 3 H), 7.43−7.52 (m, 2 H), 7.56 (dt, J = 7.80 Hz, J = 1.95 Hz, 1 H), 8.14 (d, J = 2.34 Hz, 1 H), 8.52 (dd, J = 5.07 Hz, J = 1.56 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.5, 59.9, 123.3, 124.6, 128.4, 129.7, 134.3, 138.1, 145.1, 149.8, 151.1 ppm; MS (EI): m/z (%) = 247 $[M]^+$ (30), 207 (4), 167 (5), 139 (1), 115 (1), 92 (100), 65 (30); IR: υ = 2981 (w), 1594 (m), 1479 (m), 1301 (s), 1288 (s), 1270 (s), 1193 (s), 1147 (s), 1084 (s), 1027 (m), 896 (w) cm^{-1}. The obtained data match those reported in the literature.[29]

*1-Methoxy-4-(tosylmethyl)benzene (**6ac**) [CAS: 58680-51-6].* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromoanisole (112 mg, 0.60 mmol, 75 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (136.4 mg, 0.49 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 99% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.43 (s, 3 H), 3.80 (s, 3 H), 4.24 (s, 2 H), 6.76−6.83 (m, 2 H), 6.96−7.05 (m, 2 H), 7.25 (dd, J = 8.59 Hz, J = 0.78 Hz, 2 H), 7.49−7.55 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 55.3, 62.2, 113.9, 120.2, 128.6, 129.5, 132.0, 135.1, 144.5, 159.9 ppm; MS (EI): m/z (%) = 276 $[M]^+$ (3), 228 (1), 197 (1), 164 (1), 121 (100), 91 (10); IR: υ = 2956 (w), 1607 (w), 1509 (m), 1288 (s), 1241 (s), 1178 (s), 1146 (s), 1085 (m), 1031 (m), 817 (s), 756 (s) cm^{-1}. The obtained data match those reported in the literature.[30]

*N,N-Dimethyl-4-(tosylmethyl)aniline (**6ad**) [CAS: 3933-62-9].* The compound was prepared according to method A from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromo-*N*,*N*-dimethylaniline (111 mg, 0.55 mmol), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (135.2 mg, 0.47 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 93% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.42 (s, 3 H), 2.94 (s, 6 H), 4.20 (s, 2 H), 6.55−6.62 (m, 2 H), 6.90−6.97 (m, 2 H), 7.24 (d, J = 8.20 Hz, 2 H), 7.49−7.58 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 40.3, 62.4, 112.0, 115.0,

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127.3, 128.6, 129.3, 131.5, 135.3, 150.5 ppm; MS (EI): m/z (%) = 289 $[M]^+$ (5), 224 (1), 194 (1), 178 (1), 165 (1), 134 (100), 118 (15), 91 (10); IR: υ = 2915 (s), 1617 (m), 1531 (m), 1367 (m), 1299 (m), 1287 (m), 1142 (s), 1084 (m), 946 (w), 804 (s), 729 (s) cm^{-1}. The obtained data match those reported in the literature.[31]

*4-(Tosylmethyl)thioanisole (**6ae**).* The title compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromothioanisole (122 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (145.0 mg, 0.50 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 99% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.42 (s, 3 H), 2.44−2.48 (m, 3 H), 4.24 (s, 2 H), 6.96−7.03 (m, 2 H), 7.09−7.15 (m, 2 H), 7.25 (d, J = 8.20 Hz, 2 H), 7.48−7.57 (m, 2 H); $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 15.3, 21.6, 62.3, 124.6, 126.0, 128.5, 129.5, 131.1, 134.9, 139.6, 144.6 ppm; MS (EI): m/z (%) = 292 $[M]^+$ (5), 213 (1), 184 (1), 165 (2), 137 (100), 91 (5); IR: υ = 2980 (w), 1492 (m), 1300 (s), 1288 (s), 1146 (s), 1086 (s), 812 (s), 697 (s) cm^{-1}; mp 151−153 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{16}NaO_2S_2$: 315.0484; found: 315.0492.

*2-(Tosylmethyl)-m-xylene (**6af**).* The compound was prepared according to method A from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 2-bromo-*m*-xylene (103 mg, 0.55 mmol, 74 μL), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (65.6 mg, 0.24 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 48% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.22 (s, 6 H), 2.45 (s, 3 H), 4.50 (s, 2 H), 7.02 (d, J = 7.41 Hz, 1 H), 7.10−7.17 (m, 1 H), 7.30 (d, J = 8.20 Hz, 1 H), 7.60−7.66 (m, 1 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 20.3, 21.6, 57.4, 125.5, 128.4, 128.5, 128.6, 129.7, 136.6, 139.2, 144.7 ppm; MS (EI): m/z (%) = 274 $[M]^+$ (5), 195 (1), 180 (1), 165 (2), 155 (1), 139 (1), 119 (100), 91 (20), 77 (10); IR: υ = 2926 (s), 1596 (2), 1449 (s), 1310 (m), 1143 (s), 1083 (s), 910 (w), 763 (s) cm^{-1}; mp 113−115 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{18}NaO_2S$: 297.0920; found: 297.0919.

*2-(Tosylmethyl)-o-toluene (**6ag**) [CAS: 98752-69-3].* The compound was prepared according to method A from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 2-bromotoluene (94.1 mg, 0.55 mmol, 66 μL), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (117.8 mg, 0.45 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 90% yield as a light yellow solid. ^{1}HNMR (400 MHz, $CDCl_3$) δ = 2.12 (s, 3 H), 2.42 (s, 3 H), 4.36 (s, 2 H), 6.99−7.06 (m, 1 H), 7.07−7.16 (m, 2 H)- 7.18−7.29 (m, 3 H), 7.48−7.57 (m, 2 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 19.3, 21.5, 59.9, 125. 9, 126.6, 128.5, 128.8, 129.4, 130.5, 131.8, 135.4, 138.2, 144.6 ppm; MS (EI): m/z (%) = 260 $[M]^+$ (5), 207 (1), 181 (2), 139 (1), 105 (100), 77 (10); IR: υ = 2923 (w), 1595 (w), 1451 (w), 1312 (s), 1288 (s), 1153 (s), 1132 (s), 1084 (s), 884 (w), 812 (s) cm^{-1}. The obtained data match those reported in the literature.[32]

*1-Chloro-4-(tosylmethyl)benzene (**6ah**) [CAS: 20025-49-4].* The title compound was prepared according to method A from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 1-bromo-4-chlorobenzene (105 mg, 0.55 mmol), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (55.9 mg, 0.20 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 40% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.39 (s, 3 H), 4.22 (s, 2 H), 6.96−7.03 (m, 2 H), 7.17−7.26 (m, 4 H), 7.46−7.52 (m, 2 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 21.6, 62.1, 126.8, 128.6, 128.8, 129.6, 132.0, 134.7, 134.9, 144.9 ppm; MS (EI): m/z (%) = 280 $[M]^+$ (2), 201 (1), 165 (2), 125 (100), 89 (10). IR: υ = 2932 (w), 1487 (w), 1303 (s), 1147 (s), 1085 (s), 1014 (m), 817 (s), 717 (s) cm^{-1}. The obtained data match those reported in the literature.[33]

*Ethyl 4-(Tosylmethyl)benzoate (**6ai**) [CAS: 117687-58-8].* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), ethyl 4-bromobenzoate (137 mg, 0.60 mmol, 98 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (158 mg, 0.44 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 99% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 1.40 (t, J = 7.02 Hz, 3 H), 2.43 (s, 3 H), 4.35 (s, 2 H), 4.38 (q, J = 7.02 Hz, 2 H), 7.13−7.19 (m, 2 H), 7.25 (d, J = 8.20 Hz, 2 H), 7.47−7.54 (m, 2 H), 7.90−7.98 (m, 2 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 14.2, 21.6, 61.1, 62.5, 128.5, 129. 6, 129.9, 130.6, 130.7, 133.1, 134.7, 144. 9, 166.0 ppm; MS (EI): m/z (%) = 318 $[M]^+$ (5), 273 (5), 254 (1), 209 (2), 182 (1), 163 (100), 135 (20), 107 (20); IR: υ = 2916 (w), 1710 (s), 1276 (s), 1148 (s) 1113 (s) 1086 (m), 1020 (m), 820 (m), 777 (m), 708 (s) cm^{-1}. The obtained data match those reported in the literature.[34]

*4-(Tosylmethyl)benzonitrile (**6aj**) [CAS: 59475-60-4].* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromobenzonitrile (109 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (120.6 mg, 0.50 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 89% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.45 (s, 3 H), 4.34 (s, 2 H), 7.21−7.26 (m, 2 H), 7.27−7.31 (m, 2 H), 7.49−7.55 (m, 2 H), 7.56−7.61 (m, 2 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 21.7, 62.5, 112.8, 118.2, 128.5, 129.8, 131.5, 132.2, 133.6, 134.6, 145.32 ppm; MS (EI): m/z (%) = 271 $[M]^+$ (20), 192 (5) 155 (40) 116 (100), 91 (40), 65 (30); IR: υ = 2929 (w), 2227 (w), 1311 (s), 1291 (s), 1147 (s), 1085 (m), 819 (s) 736 (s) cm^{-1}. The obtained data match those reported in the literature.[33]

*1-Nitro-4-(tosylmethyl)benzene (**6ak**) [CAS: 61081-32-1].* The title compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromo-1-nitrobenzene (121 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (130 mg, 0.45 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 89% yield as a light yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.45 (s, 3 H), 4.39 (s, 2 H), 7.28−7.34 (m, 4 H), 7.50−7.59 (m, 2 H), 8.09−8.19 (m, 2 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 21.7, 62.2, 123.7, 128.5, 129.9, 131.8, 134. 6, 135.5, 145.4, 148.1 ppm; MS (EI): m/z (%) = 291 $[M]^+$ (40), 261 (1), 227 (5), 197 (1), 178 (3), 155 (100), 136 (75), 111 (35), 91 (90), 65 (30); IR: υ = 2923 (w), 1596 (m), 1512 (s), 1340 (s), 1301 (s), 1289 (s), 1145 (s), 1085 (s), 857 (m), 699 (s) cm^{-1}. The obtained data match those reported in the literature.[28]

*4-(Tosylmethyl)benzaldehyde (**6al**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromobenzaldehyde (111 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (52.1 mg, 0.19 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 38% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.34 (s, 3 H), 4.28 (s, 2 H), 7.18 (t, J = 8.39 Hz, 4 H), 7.40−7.45 (m, 2 H), 7.65−7.72 (m, 2 H), 9.91 (s, 1 H) ppm; $^{13}C\{1H\}$NMR (100 MHz, $CDCl_3$) δ = 21.6, 62.7, 128.5, 129.7, 131.5, 134.7, 134.8, 136.2, 145.1, 191.6 ppm; MS (EI): m/z (%) = 274 $[M]^+$ (30), 195 (3), 165 (10), 139 (5), 119 (100), 91 (75), 65 (25); IR: υ = 2849 (w), 1691 (s), 1604 (m), 1303 (s) 1290 (s), 1205 (w), 1145 (s), 1083 (m), 817 (s), 740 (s) cm^{-1}; mp 155−157 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{14}NaO_3S$: 297.0556; found: 297.0554.

*3-(Tosylmethyl)furan (**6am**) [CAS: 92631-12-4].* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 3-bromofuran (111 mg, 0.60 mmol, 54 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (60.6 mg, 0.26 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 51% yield as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ = 2.32 (s, 3 H), 4.06 (s, 2 H), 6.19 (dd, J = 1.95 Hz, J = 0.78 Hz, 1 H), 7.11 (dd, J = 1.56 Hz, J = 0.78

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Hz, 1 H), 7.15−7.21 (m, 2 H), 7.25 (t, J = 1.76 Hz, 1 H), 7.46−7.55 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 53.3, 111.5, 112.7, 128.5, 129.6, 134.8, 142.7, 143.3 ppm; MS (EI): m/z (%) = 236 $[M]^+$ (5), 190 (1), 172 (25), 147 (10), 128 (10), 101 (15), 81 (100); IR: υ = 2922 (w), 1594 (w), 1381 (w), 1308 (s), 1274 (s), 1235 (m), 1148 (s), 1124 (s), 1017 (s), 871 (s), 805 (s) cm^{-1}. The obtained data match those reported in the literature.[35]

*2-(Tosylmethyl)thiophene (**6an**) [CAS: 20895-79-8].* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 2-bromothiophene (97.8 mg, 0.60 mmol, 58 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (38.8 mg, 0.15 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 31% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.34 (s, 3 H), 4.42 (s, 2 H), 6.77 (d, J = 3.51 Hz, 1 H), 6.85 (dd, J = 5.27 Hz, J = 3.71 Hz, 1 H), 7.14−7.21 (m, 3 H), 7.46−7.52 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 57.3, 127.1, 127.4, 128.6, 128.7, 129.6, 130.1, 134.5, 144.9 ppm; MS (EI): m/z (%) = 252 $[M]^+$ (5), 207 (1), 187 (5), 155 (3), 129 (5), 97 (100), 65 (10); IR: δ = 2969 (w), 1593 (w), 1403 (w), 1310 (s), 1303 (s), 1288 (s), 1144 (s), 1081 (m), 814 (m), 719 (s) cm^{-1}. The obtained data match those reported in the literature.[36]

*2-Ethoxy-5-(tosylmethyl)pyridine (**6ao**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 3-bromo-2-ethoxypyridine (121 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (141.2 mg, 0.49 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 97% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.35 (t, J = 7.02 Hz, 3 H), 2.40 (s, 3 H), 4.19 (s, 2 H), 4.29 (q, J = 7.02 Hz, 2 H), 6.64 (d, J = 8.59 Hz, 1 H), 7.20−7.28 (m, 2 H), 7.41 (dd, J = 8.59 Hz, J = 2.73 Hz, 1 H), 7.48−7.55 (m, 2 H), 7.69 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 14.4, 21.6, 59.4, 61.9, 110.9, 116.9, 128.5, 129.6, 134.6, 140.5, 144.9, 148.6, 164.0 ppm; MS (EI): m/z (%) = 291 (3), 233 (1), 212 (1), 181 (1), 155 (2), 136 (100), 108 (75), 80 (20); IR: υ = 2980 (w), 1732 (w), 1607 (w), 1476 (s), 1400 (w), 1379 (m), 1303 (s), 1287 (s), 1260 (m), 1144 (s), 925 (m), 818 (m), 728 (s) cm^{-1}; mp 115−117 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{15}H_{17}NNaO_3S$: 314.0823; found: 314.0821.

*2-Methyl-5-(tosylmethyl)pyridine (**6ap**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 3-bromo-2-metylpyridine (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (108.3 mg, 0.41 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 83% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.38 (s, 3 H), 2.50 (s, 3 H), 4.22 (s, 2 H), 7.08 (d, J = 8.20 Hz, 1 H), 7.23 (d, J = 7.81 Hz, 2 H), 7.45 (dd, J = 8.00 Hz, J = 2.15 Hz, 1 H), 7.50 (d, J = 8.20 Hz, 2 H), 8.00 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.5, 24.1, 59.6, 121.4, 123.00, 128.4, 129.7, 134.5, 138.3, 145.0, 150.4, 158.8 ppm; MS (EI): m/z (%) = 261 $[M]^+$ (10), 214 (1), 182 (3), 155 (1), 125 (1), 106 (100), 77 (25); IR: υ = 2923 (w), 1597 (m) 1488 (m), 1310 (s), 1258 (m), 1148 (s), 1085 (s), 1030 (m), 813 (s), 723 (s) cm^{-1}; mp 97−99 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{14}H_{15}NNaO_2S$: 284.0716; found: 284.0717.

*2-Chloro-5-(tosylmethyl)pyridine (**6aq**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 3-bromo-5-chloropyridine (115 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (50.0 mg, 0.18 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 35% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.44 (s, 3 H), 4.26 (s, 2 H), 7.27−7.33 (m, 2 H), 7.51−7.57 (m, 2 H), 7.60 (t, J = 2.15 Hz, 1 H), 8.05 (d, J = 1.95 Hz, 1 H), 8.52 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 59.3, 125.8, 128.5, 129.9, 131.9, 134.2, 137.7, 145.5, 148.9, 148.9 ppm; MS (EI): m/z (%) = 281 $[M]^+$ (60), 246 (1), 217 (5), 180 (1), 155 (40), 126 (100), 91 (50), 65 (20); IR: υ = 2916 (w), 1594 (w), 1424 (m), 1307 (s), 1258 (s), 1141 (s), 1121 (s), 1185 (m), 1021 (m), 893 (m), 755 (s), 713 (s) cm^{-1}; mp 123−125 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{13}H_{12}ClNNaO_2S$: 304.0169; found: 304.0171.

*2-(N-Boc-piperazinyl)-5-(tosylmethyl)piperidine (**6ar**).* The title compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 5-bromo-2-(*N*-boc-piperazinyl)pyridine (205 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (214 mg, 0.50 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 99% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.49 (s, 9 H), 2.42 (s, 3 H), 3.52 (s, 8 H), 4.15 (s, 2 H), 6.57 (d, J = 8.59 Hz, 1 H), 7.27 (d, J = 7.41 Hz, 2 H), 7.37 (dd, J = 8.78 Hz, J = 2.54 Hz, 1 H), 7.52−7.60 (m, 2 H), 7.74 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 28.3, 44.7, 59.5, 79.9, 106. 6, 113.0, 128. 5, 129.6, 134.9, 139.6, 144.7, 149.6, 154.7, 158.9 ppm; MS (EI): m/z (%) = 403 $[M - CH_3]^+$ (10), 386 (20), 345 (10), 263 (8), 176 (100), 134 (10), 91 (5); IR: υ = 2977 (w), 1691 (s), 1603 (s), 1496 (s), 1407 (s), 1238 (s), 1163 (s),1121 (s), 1083 (m), 934 (m), 811 (m), 769 (m) cm^{-1}; mp 136−138 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{22}H_{29}N_3NaO_4S$: 454.1771; found: 454.1780.

*3-(Tosylmethyl)quinoline (**6as**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 3-bromoquinoline (104 mg, 0.60 mmol, 68 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (105.9 mg, 0.36 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 71% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.42 (s, 3 H), 4.48 (s, 2 H), 7.26 (d, J = 7.80 Hz, 2 H), 7.51−7.56 (m, 2 H), 7.56−7.62 (m, 1 H), 7.72−7.82 (m, 2 H), 8.05−8.11 (m, 2 H), 8.42 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.7, 60.2, 121.6, 127.2, 127.5, 127.9, 128.6, 129.3, 129.9, 130.3, 134.6, 138.3, 145.3, 147.7, 151.4 ppm; MS (EI): m/z (%) = 297 $[M]^+$ (3), 256 (100), 227 (10), 200 (8), 163 (1), 142 (40), 115 (10), 88 (8); IR: υ = 2971 (w), 1739 (w), 1493 (m), 1300 (s), 1145 (s), 1084 (s), 908 (m), 818 (s), 742 (s), 699 (s) cm^{-1}; mp 144−146 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{15}NNaO_2S$: 320.0716; found: 320.0710.

*2-(Tosylmethyl)pyridine (**6at**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 2-bromopyridine (94.8 mg, 0.60 mmol, 57 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (22.8 mg, 0.09 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 18% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.71 (s, 3 H), 4.82 (s, 2 H), 7.49−7.57 (m, 4 H), 7.76 (d, J = 7.81 Hz, 1 H), 7.80−7.86 (m, 2 H), 7.99 (td, J = 7.71 Hz, J = 1.76 Hz, 1 H), 8.72 (dd, J = 3.90 Hz, J = 0.78 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 64.7, 123.3, 125.8, 128.4, 129.6, 135.4, 136.7, 144. 8, 149.1, 149.6 ppm; MS (EI): m/z (%) = 246 $[M - H]^+$ (1), 220 (1), 201 (1), 182 (100), 158 (1), 139 (1), 92 (30), 65 (35); IR: υ = 2969 (w), 1585 (w), 1473 (w), 1434 (m), 1379 (m), 1298 (s), 1148 (s), 1084 (s), 792 (s), 726 (s) cm^{-1}; mp 131−133 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{13}H_{13}NNaO_2S$: 270.0559; found: 270.0559.

*5-Cyano-2-(tosylmethyl)pyridine (**6au**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 2-bromo-5-cyanopyridine (110 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product was obtained along with nonconverted 2-bromo-5-cyanopyridine which could not be separated by column chromatography (silica gel, heptane/ethyl acetate gradient). The mixture contains the product in 24% yield (32.6 mg, 0.12 mmol) by ^{1}H NMR with mesitylene as an internal standard. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.43 (s, 3 H), 4.59 (s, 2 H), 7.26−7.31 (m, 2 H), 7.55 (d, J = 8.20 Hz, 2 H), 8.68 (m, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 64.5, 109.6, 116.1, 125.6, 128.3, 129.8, 135.00, 139. 8, 145.4, 153.2, 154.3 ppm; MS

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(EI): m/z (%) = 272 $[M]^+$ (1), 245 (1), 207 (100), 176 (1), 155 (5), 117 (10), 91 (65).

*N-Methyl-5-(tosylmethyl)-7-azaindole (**6av**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 5-bromo-*N*-methyl-7-azaindole (127 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (135 mg, 0.45 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 90% yield as light brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.38 (s, 3 H), 3.83 (s, 3 H), 4.37 (s, 2 H), 6.40 (d, J = 3.51 Hz, 1 H), 7.18 (d, J = 3.51 Hz, 1 H), 7.20 (d, J = 7.80 Hz, 2 H), 7.45−7.52 (m, 2 H), 7.78 (d, J = 1.95 Hz, 1 H), 7.83 (d, J = 1.95 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.5, 31.2, 60.5, 99.5, 115.6, 120.2, 128. 5, 129. 6, 130.0, 130.9, 134.7, 144.4, 144.7, 147.6 ppm; MS (EI): m/z (%) = 300 $[M]^+$ (5), 281 (1), 235 (2), 206 (1), 164 (1), 145 (100), 117 (5), 91 (5), 65 (5); IR: υ = 2970 (w), 1597 (w), 1513 (m), 1400 (m), 1352 (m), 1308 (s), 1144 (s), 1082 (s), 818 (s), 721 (s) cm^{-1}; mp 147−149 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{16}H_{16}N_2NaO_2S$: 323.0825; found: 323.0823.

*5-(Tosylmethyl)pyrimidine (**6aw**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 5-bromopyrimidine (95.4 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (12.3 mg, 0.05 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 10% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.45 (s, 3 H), 4.28 (s, 2 H), 7.32 (d, J = 8.20 Hz, 2 H), 7.56 (d, J = 8.20 Hz, 2 H), 8.48 (s, 2 H), 9.18 (s, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.7, 57.6, 123.3, 128.5, 130.1, 134.1, 145.8, 158.2, 158.7 ppm; MS (EI): m/z (%) = 248 $[M]^+$ (80), 207 (1), 183 (2), 155 (90), 91 (100), 66 (40); IR: υ = 2920 (w), 1587 (w), 1562 (s), 1439 (m), 1412 (s), 1307 (s), 1147 (s), 1084 (s), 922 (w), 881 (m), 752 (s), 729 (m) cm^{-1}; mp 124−126 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{12}H_{12}N_2NaO_2S$: 271.0512; found: 270.0511.

*N-Methyl-4-(tosylmethyl)pyrazole (**6ax**).* The compound was prepared according to method B from *p*-tolyl methyl sulfone (85.1 mg, 0.50 mmol), 4-bromo-*N*-methylpyrazole (96.6 mg, 0.60 mmol, 62 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (26.3 mg, 0.11 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 21% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.43 (s, 3 H), 3.86 (s, 3 H), 4.18 (s, 2 H), 7.10 (s, 1 H), 7.29 (d, J = 8.20 Hz, 2 H), 7.37 (s, 1 H), 7.55−7.63 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.6, 39.1, 53.0, 107.9, 128.5, 129.6, 131.1, 134.1, 140.1, 144.7 ppm; MS (EI): m/z (%) = 250 $[M]^+$ (2), 207 (2), 171 (1), 128 (1), 95 (100), 65 (5); IR: υ = 2970 (w), 1378 (s), 1298 (s), 1254 (s), 1216 (m), 1151 (s), 1124 (s), 1085 (m), 890 (s), 759 (s) cm^{-1}; mp 86−88 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{12}H_{14}N_2NaO_2S$: 273.0668; found: 273.0666.

*4-(4-Methylbenzylsulfonyl)anisole (**6ba**) [CAS: 108545-54-6].* The compound was prepared according to method B from *p*-anisyl methyl sulfone (93.1 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (132 mg, 0.48 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 95% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.32 (s, 3 H), 3.85 (s, 3 H), 4.24 (s, 2 H), 6.86−6.93 (m, 2 H), 6.94−7.00 (m, 2 H), 7.07 (d, J = 8.20 Hz, 2 H), 7.50−7.57 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.1, 55.5, 62.7, 113.9, 125.2, 129.1, 129.5, 130.6, 130.7, 138.5, 163.6 ppm; MS (EI): m/z (%) = 276 $[M^+]$ (3), 233 (1), 212 (2), 178 (1), 155 (1), 126 (1), 105 (100), 77 (15); IR: υ = 2969 (w), 1592 (m), 1496 (m), 1296 (s), 1258 (s), 1135 (s), 1086 (s), 1017 (m), 817 (s), 665 (s) cm^{-1}. The obtained data match those reported in the literature.[37]

*1-Chloro-4-(4-methylbenzylsulfonyl)benzene (**6ca**) [CAS: 108545-52-4].* The compound was prepared according to method A from *p*-chlorophenyl methyl sulfone (97.3 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (73.9 mg, 0.26 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 53% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.33 (s, 3 H), 4.28 (s, 2 H), 6.97 (d, J = 8.02 Hz, 2 H), 7.09 (d, J = 7.83 Hz, 2 H), 7.38−7.45 (m, 2 H), 7.52−7.59 (m, 2 H) ppm; ^{13}C{1H}NMR (101 MHz, $CDCl_3$) δ = 21.2, 62.5, 124.6, 129.1, 129.3, 130.1, 130.6, 136. 4, 138.8, 140.3 ppm; MS (EI): m/z (%) = 280 $[M]^+$ (5), 215 (1), 201 (1), 178 (1), 165 (1) 142 (1), 105 (100), 89 (2), 77 (10); IR: υ = 2916 (w), 1511 (w), 1476 (w), 1393 (w), 1311 (m), 1274 (m), 1149 (s), 1086 (s), 1013 (m), 831 (s), 770 (s), 744 (m) cm^{-1}. The obtained data match those reported in the literature.[37]

*1-Fluoro-4-(4-methylbenzylsulfonyl)benzene (**6da**) [CAS: 1494-30-0].* The compound was prepared according to method A from *p*-fluorophenyl methyl sulfone (87.1 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (132 mg, 0.50 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 99% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.27−2.37 (m, 3 H), 4.27 (s, 2 H), 6.92−6.99 (m, 2 H), 7.04−7.15 (m, 4 H), 7.59−7.67 (m, 2 H) ppm; ^{13}C{1H}NMR (101 MHz, $CDCl_3$) δ = 21.2, 62.7, 116.1 (d, $^2J_{C-F}$ = 22.50 Hz), 124.8, 129.3, 130.6, 131.5 (d, $^3J_{C-F}$ = 9.54 Hz), 133. 9, 138.8, 165.7 (d, $^1J_{C-F}$ = 256.80 Hz) ppm; ^{19}F NMR (377 MHz, $CDCl_3$) δ = −103.6 (m) ppm; MS (EI): m/z (%) = 264 $[M]^+$ (2), 216 (1), 196 (1), 170 (1), 159 (1), 143 (1), 115 (1), 105 (100), 95 (10), 77 (15); IR: υ = 2922 (w), 1590 (s), 1494 (s), 1406 (w), 1314 (s), 1287 (s), 1232 (s), 1146 (s), 1085 (s), 842 (s), 820 (s), 760 (s) cm^{-1}.

*1-Methyl-4-(1-p-tolylethylsulfonyl)benzene (**6ea**) [CAS: 1244620-48-1].* The compound was prepared according to method A from *p*-tolyl ethyl sulfone (92.1 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (5.75 mg, 0.01 mmol), XPhos (4.77 mg, 0.01 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (110 mg, 0.40 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 81% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.72 (d, J = 7.02 Hz, 3 H), 2.33 (s, 3 H), 2.40 (s, 3 H), 4.19 (q, J = 7.02 Hz, 1 H), 7.01−7.09 (m, 4 H), 7.20 (d, J = 7.81 Hz, 2 H), 7.41−7.49 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 14.1, 21.1, 21.5, 65.6, 128.9, 129.2, 129.2, 129.2, 130.7, 133.9, 138.5, 144.3 ppm; MS (EI): m/z (%) = 273 $[M]^+$ (1), 195 (1), 165 (1), 139 (1), 119 (100), 91 (20), 65 (10); IR: υ = 2927 (w), 1512 (w), 1448 (w), 1378 (m), 1298 (s), 1140 (s), 1084 (m), 1042 (m), 816 (m), 144 (m) cm^{-1}. The obtained data match those reported in the literature.[31]

*(p-Methyl-benzyl) Methyl Sulfoxide (**6ga**) [CAS: 5936-94-7].* The title compound was prepared according to method B from dimethyl sulfone (47.1 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (90.3 mg, 0.49 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 98% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.38 (s, 3 H), 2.75 (s, 3 H), 4.22 (s, 2 H), 7.19−7.25 (m, 2 H), 7.28−7.33 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.2, 38.82, 61.0, 125.2, 129. 8, 130.3, 139.2 ppm; MS (EI): m/z (%) = 184 $[M]^+$ (5), 105 (100), 77 (15); IR: υ = 2923 (w), 1515 (w), 1452 (w), 1302 (s), 1258 (m), 1159 (m), 1120 (s), 975 (w), 888 (m), 821 (m), 758 (w) cm^{-1}. The obtained data match those reported in the literature.[38]

*N-((1-(p-Tolyl)ethyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**10aa**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (113 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (125 mg, 0.40 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 79% yield as a light yellow oil. ^{1}H NMR (400 MHz,

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$CDCl_3$) δ = 1.43 (m, 1 H), 1.71 (m, 1 H), 1.83 (d, J = 7.02 Hz, 3 H), 2.36 (s, 3 H), 2.43−2.53 (m, 1 H), 2.63−2.73 (m, 1 H), 3.08−3.17 (m, 1 H), 3.42−3.53 (m, 1 H), 4.55 (q, J = 7.02 Hz, 1 H), 6.99−7.04 (m, 1 H), 7.05−7.09 (m, 1 H), 7.12 (s, 4 H), 7.14−7.20 (m, 1 H), 7.60 (d, J = 8.20 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.5, 21.1, 22.1, 27.1, 47.3, 62.0, 120.2, 123.1, 126.5, 128.0, 129.0, 129.1, 129.7, 131.3, 137.3, 138.7 ppm; MS (EI): m/z (%) = 315 $[M]^+$ (1), 281 (1), 251 (20), 298 (1), 180 (1), 160 (1), 139 (55), 119 (100), 91 (10); IR: υ = 2937 (w), 1513 (w), 1489 (s), 1453 (m), 1331 (s), 1235 (m), 1145 (s), 1087 (m), 978 (m), 910 (m), 850 (s), 728 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{21}NNaO_2S$: 338.1185; found: 338.1186.

*N-((1-(p-Anisyl)ethyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**10ab**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (113 mg, 0.50 mmol), 4-bromoanisole (112 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (98.4 mg, 0.30 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 59% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.35−1.49 (m, 1 H), 1.71 (m, 1 H), 1.81 (d, J = 7.02 Hz, 3 H), 2.42−2.54 (m, 1 H), 2.61−2.74 (m, 1 H), 3.06−3.17 (m, 1 H), 3.41−3.52 (m, 1 H), 3.75−3.84 (m, 3 H), 4.52 (q, J = 7.02 Hz, 1 H), 6.79−6.86 (m, 2 H), 6.98−7.04 (m, 1 H), 7.04−7.09 (m, 1 H), 7.10−7.19 (m, 3 H), 7.59 (d, J = 8.20 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.6, 22.2, 27.2, 47.3, 55.3, 61.7, 113.8, 120.2, 123.1, 126.3, 126.5, 128.0, 129.7, 130.4, 137.3, 159.9 ppm; MS (EI): m/z (%) = 331 $[M]^+$ (1), 267 (15), 238 (1), 217 (1), 194 (1), 154 (1), 135 (100), 105 (20), 77 (10); IR: υ = 2937 (w), 1609 (w), 1512 (s), 1488 (s), 1453 (s), 1330 (s), 1249 (s), 1179 (s), 1143 (s), 1086 (m), 1023 (s), 833 (s), 753 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{21}NNaO_3S$: 354.1134; found: 354.1127.

*N-((1-(4-Trifluoromethylphenyl)ethyl)sulfonyl)-1,2,3,4-tetrhydroquinoline (**10ac**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydro-quinoline (113 mg, 0.50 mmol), 4-bromobenzotrifluoride (135 mg, 0.60 mmol, 84 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (126 mg, 0.34 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 68% yield as a colorless solid that crystallized slowly. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.37−1.50 (m, 1 H), 1.69−1.81 (m, 1 H), 1.85 (d, J = 7.02 Hz, 3 H), 2.42−2.50 (m, 1 H), 2.65−2.73 (m, 1 H), 3.19−3.25 (m, 1 H), 3.47−3.57 (m, 1 H), 4.63 (q, J = 7.28 Hz, 1 H), 6.99−7.09 (m, 2 H), 7.16 (m, 1 H), 7.37 (d, J = 8.20 Hz, 2 H), 7.52−7.60 (m, 3 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.7, 22.3, 27.1, 47.4, 62.0, 120.4, 123.7, 123.8 (q, $^1J_{C-F}$ = 272.16 Hz), 125.4 (q, $^3J_{C-F}$ = 3.91 Hz), 126.7, 128.2, 129.7, 129.9, 131.0 (q, $^2J_{C-F}$ = 32.28 Hz), 137.0, 138.5 (q, $^4J_{C-F}$ = 1.47 Hz) ppm; ^{19}F NMR (377 MHz, $CDCl_3$) δ = −62.8 (s) ppm; MS (EI): m/z (%) = 369 $[M]^+$ (15), 290 (50), 262 (2), 197 (2), 173 (85), 153 (40), 133 (100), 103 (20) 77 (25); IR: υ = 2940 (w), 1489 (m), 1454 (w), 1418 (w), 1322 (s), 1146 (s), 1116 (s), 1087 (s), 1068 (s), 1018 (m), 978 (m), 845 (s), 753 (s) cm^{-1}; mp 64−66 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{18}F_3NNaO_2S$: 392.0903; found: 392.0899.

*N-((1-(4-Nitrophenyl)ethyl)sulfonyl)-1,2,3,4-tetrahydroquinoline (**10ad**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (113 mg, 0.50 mmol), 4-bromo-1-nitrobenzene (121 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (133 mg, 0.38 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 77% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.48−1.54 (m, 1 H), 1.73−1.83 (m, 1 H), 1.85 (d, J = 7.02 Hz, 3 H), 2.46−2.54 (m, 1 H), 2.68−2.75 (m, 1 H), 3.21−3.27 (m, 1 H), 3.52−3.61 (m, 1 H), 4.67 (q, J = 7.28 Hz, 1 H), 7.00−7.11 (m, 2 H), 7.14−7.20 (m, 1 H), 7.41−7.47 (m, 2 H), 7.57 (d, J = 8.20 Hz, 1 H), 8.12−8.20 (m, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.7, 22.4, 27.1, 47.4, 61.8, 120.4, 123.6, 123.8, 126. 8, 128.2, 129.9, 130.2, 136.8, 141.6, 148.0 ppm; MS (EI): m/z (%) = 346 $[M]^+$ (25), 267 (65), 236 (5), 197 (2), 151 (50), 132 (100), 104 (30), 77 (28); IR: υ = 2941 (w), 1520 (s), 1488 (s), 1453 (m), 1339 (s), 1235 (m), 1145 (s), 1119 (m), 1042 (m), 978 (m), 853 (s), 755 (s), 695 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{18}N_2NaO_4S$: 369.0879; found: 369.0881.

*N-(1-(6-Methylpyridin-3-yl)ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (**10ae**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (113 mg, 0.50 mmol), 5-bromo-2-methylpyridine (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (19.6 mg, 0.06 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 19% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.22−1.31 (m, 2 H), 1.42−1.46 (m, 2 H), 1.67−1.80 (m, 2 H), 1.82 (d, J = 7.02 Hz, 3 H), 2.55 (s, 3 H), 2.64−2.75 (m, 1 H), 3.20−3.26 (m, 1 H), 3.47−3.57 (m, 1 H), 4.54 (q, J = 7.41 Hz, 1 H), 6.94−7.11 (m, 2 H), 7.11−7.18 (m, 2 H), 7.58 (d, J = 8.59 Hz, 1 H), 7.63 (dd, J = 8.20 Hz, J = 2.34 Hz, 1 H), 8.14 (d, J = 2.34 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.5, 22.3, 24.1, 27.1, 47.3, 59.6, 120.2, 120.4, 123.2, 123.6, 126.7, 128.3, 130.0, 136.6, 136.9, 149.7, 159.1 ppm; MS (EI): m/z (%) = 316 $[M]^+$ (10), 280 (1), 252 (30), 196 (2), 160 (1), 138 (75), 120 (100), 96 (10), 77 (20); IR: υ = 2930 (w), 1600 (w), 1489 (s), 1452 (m), 1333 (s), 1235 (w), 1145 (s), 1086 (m), 1021 (m), 978 (m), 849 (s), 754 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{17}H_{20}N_2NaO_2S$: 339.1138; found: 339.1135.

*1-(1-(6-Isopropoxypyridin-3-yl)ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (**10af**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydro-quinoline (113 mg, 0.50 mmol), 5-bromo-2-isopropoxy pyridine (130 mg, 0.60 mmol, 94 μL), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (73.4 mg, 0.20 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 41% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.33 (d, J = 6.24 Hz, 6 H), 1.41−1.52 (m, 1 H), 1.71−1.78 (m, 1 H), 1.80 (d, J = 7.02 Hz, 3 H), 2.47−2.59 (m, 1 H), 2.65−2.76 (m, 1 H), 3.25−3.30 (m, 1 H), 3.48−3.58 (m, 1 H), 4.49 (q, J = 7.02 Hz, 1 H), 5.25 (quin., J = 6.24 Hz, 1 H), 6.65 (d, J = 8.59 Hz, 1 H), 6.97−7.03 (m, 1 H), 7.04−7.09 (m, 1 H), 7.10−7.17 (m, 1 H), 7.53−7.61 (m, 2 H), 7.76 (d, J = 2.73 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.4, 21.9, 22.3, 27.1, 47.3, 59.3, 68.3, 111.6, 120.3, 122.6, 123.5, 126.6, 128.1, 129.9, 137.1, 138.7, 147. 7, 163.7 ppm; MS (EI): m/z (%) = 369 $[M]^+$ (1), 346 (1), 317 (1), 296 (15), 239 (1), 196 (91), 164 (45), 142 (30), 122 (100), 94 (15), 67 (5); IR: υ = 2977 (w), 2936 (w), 1604 (s), 1484 (s), 1333 (s), 1306 (s), 1281 (s), 1144 (s), 1105 (s), 1018 (m), 948 (m), 847 (s), 753 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{24}N_2NaO_3S$: 383.1400; found: 383.1401.

*N-(1-(N-Methyl-7-azaindol-5-yl)ethylsulfonyl)-1,2,3,4-tetrahydroquinoline (**10ag**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-1,2,3,4-tetrahydro-quinoline (113 mg, 0.50 mmol), *N*-methyl-5-bromo-7-azaindole (127 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (93.1 mg, 0.26 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 52% yield as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.26−1.32 (m, 1 H), 1.58−1.70 (m, 1 H), 1.89 (d, J = 7.02 Hz, 3 H), 2.33−2.47 (m, 1 H), 2.56−2.68 (m, 1 H), 3.01−3,07 (m, 1 H), 3.38−3.48 (m, 1 H), 3.82−3.89 (m, 3 H), 4.69 (q, J = 7.28 Hz, 1 H), 6.43 (d, J = 3.51 Hz, 1 H), 6.95−7.02 (m, 1 H), 7.02−7.08 (m, 1 H), 7.11−7.17 (m, 1 H), 7.20 (d, J = 3.51 Hz, 1 H), 7.63 (d, J = 8.20 Hz, 1 H), 7.89 (d, J = 1.95 Hz, 1 H), 8.01 (d, J = 1.95 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 15.9, 22.2, 27.0, 31.3, 47.2, 60.3, 99.6, 120.1, 120.2, 121.8, 123.3, 126.5, 128.1, 129.0, 129.8, 130.1, 137.1, 143.8, 147.8 ppm; MS (EI): m/z (%) = 355 $[M]^+$ (2), 291 (10), 243 (1), 191 (1), 159 (100), 133 (20), 103 (10), 77 (5); IR: υ = 2939 (w), 1515 (w), 1489 (m), 1453 (w). 1329 (s), 1234 (m), 1329 (s), 1234 (m), 1144 (s), 1085 (m), 979 (m), 906 (s), 850 (m), 720 (s) cm^{-1}. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{22}N_3O_2S$: 356.1427; found: 356.1423.

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*N-(1-p-Tolylethylsulfonyl)-2,3,4,5-tetrahydrobenzoazepine (**10ba**).* The compound was prepared according to method B from *N*-(ethylsulfonyl)-2,3,4,5-tetrahydrobenzoazepine (120 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (153 mg, 0.46 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 93% yield as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.77 (d, J = 7.02 Hz, 3 H), 2.34 (s, 3 H), 2.76−2.94 (m, 4 H), 2.96−3.24 (m, 4 H), 4.18 (q, J = 7.28 Hz, 1 H), 7.02−7.09 (m, 2 H), 7.10−7.17 (m, 4 H), 7.26 (d, J = 8.20 Hz, 2 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 16.0, 21.2, 39.1, 48.8, 62.9, 126.5, 128.8, 129.3, 129.6, 132.0, 134.3, 138.6, 140.8 ppm; MS (EI): m/z (%) = 329 $[M]^+$ (1), 250 (60), 174 (5), 147 (15), 119 (100), 91 (20); IR: υ = 2913 (w), 1514 (w), 1450 (w), 1357 (w), 1322 (s), 1307 (s), 1140 (s), 1083 (m), 1032 (m), 937 (w), 893 (s), 822 (s), 728 (s) cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{23}NNaO_2S$: 352.1342; found: 352.1338.

*N-(2-Methoxypyridin-3-yl)-1-p-tolyl-N-((2-(trimethylsilyl)ethoxy)-methyl)ethanesulfonamide (**10ca**).* The compound was prepared according to method B from *N*-(2-methoxypyridin-3-yl)-*N*-((2-(trimethylsilyl)ethoxy)methyl)ethanesulfonamide (173 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (142 mg, 0.33 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 65% yield as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = −0.01 (s, 9 H), 0.78−0.88 (m, 2 H), 1.77 (d, J = 7.41 Hz, 3 H), 2.36 (s, 3 H), 3.63 (t, J = 8.39 Hz, 2 H), 4.05 (s, 3 H), 4.21 (d, J = 7.41 Hz, 1 H), 4.61−4.80 (m, 2 H), 6.91 (dd, J = 7.61 Hz, J = 4.88 Hz, 1 H), 7.18 (d, J = 7.80 Hz, 2 H), 7.37 (d, J = 8.20 Hz, 2 H), 7.47−7.55 (m, 1 H), 8.14 (dd, J = 4.88 Hz, J = 1.76 Hz, 1 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = −1. 5, 21.2, 22.7, 31.9, 53.6, 64.2, 65.2, 79.4, 117.3, 121.3, 129.1, 129.3, 131.6, 138.6, 142.2, 146.6, 159.8 ppm; MS (EI): m/z (%) = 436 $[M]^+$ (1), 407 (1), 378 (5), 343 (2), 299 (2), 260 (20), 241 (40), 196 (10), 165 (2), 138 (20), 119 (100), 93 (10), 73 (40); IR: υ = 2052 (w), 1586 (w), 1469 (s), 1409 (s), 1340 (s) 1300 (m), 1248 (m), 1214 (m), 1157 (s), 1079 (s), 1014 (s), 908 (s), 822 (s), 728 (s), cm^{-1}; HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{32}N_2NaO_4SSi$: 459.1744; found: 459.1745.

*N,N-Diphenyl-1-p-tolylmethanesulfonamide (**10da**).* The compound was prepared according to method B from *N,N*-diphenylmethanesulfonamide (124 mg, 0.50 mmol), 4-bromotoluene (103 mg, 0.60 mmol), $Pd(dba)_2$ (28.8 mg, 0.05 mmol), XPhos (25.1 mg, 0.05 mmol), and tmp·ZnCl·LiCl solution (2.5 M, 1.25 mmol, 5.0 mL). The desired product (54.6 mg, 0.16 mmol) was obtained after chromatography (silica gel, heptane/ethyl acetate gradient) in 32% yield as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.36 (s, 3 H); 4.40 (s, 2 H); 7.06−7.12 (m, 4 H), 7.15−7.28 (m, 10 H) ppm; ^{13}C{1H}NMR (100 MHz, $CDCl_3$) δ = 21.2, 57.6, 125.4, 126.8, 127.5, 129.2, 129.5, 131.0, 138. 9, 141.2 ppm, MS (EI): m/z (%) = 337 $[M]^+$ (3), 295 (1), 273 (50), 243 (1), 222 (1), 190 (2), 167 (20), 139 (5), 105 (100), 77 (20) cm^{-1}; IR: υ = 2971 (w), 1588 (w), 1486 (s), 1338 (s), 1251 (m), 1156 (s), 1130 (s), 1028 (m), 962 (s), 903 (m), 866 (m), 828 (m), 756 (s) cm^{-1}; mp 103−105 °C. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{20}H_{19}NNaO_2S$: 360.1029; found: 360.1031.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01062.

^{1}H, ^{13}C, and ^{19}F NMR spectral data of all compounds are reported (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: thomas.knauber@pfizer.com.

Notes

The authors declare no competing financial interest.

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