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RuHCl(CO)(PPh₃)₃-Catalyzed Direct Amidation of Arene C–H Bond with Azides

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ABSTRACT: We first report the direct ortho C-H amidation of arenes with azides by using a novel and inexpensive RuHCl(CO)(PPh₃)₃

catalyst. The reaction proceeds efficiently in high yield over a broad range of substrates without requirement of any additional silver salt or additive.

INTRODUCTION

Arylamines are well established as privileged scaffolds found in a range of biological active products¹ and materials-oriented aromatics.² As a result, the development of efficient and environment-friendly methods for constructing aromatic $C(sp^2)$ –N bonds has been recognized as one of the primary issues in synthetic chemistry for long time.³ Among them, transition-metal-catalyzed *N*-arylation of aryl bromides or aryl iodides with amines has been developed as a powerful route to aminoarenes under various conditions.⁴ However, this strategy generates stoichiometric amounts of hydrogen halides or their base salts. Therefore, developing a direct amination of arene C-H bonds has been the focus of intensive research.



In recent years, a variety of transition-metals, such as rhodium(III),⁵ iridium(III)⁶ and ruthenium(II)^{7, 8} have been employed to catalyze direct C-H amination by using azides as N atom sources (Scheme 1a). The metal-catalyzed C-N bond coupling reaction proceeds in the absence of external oxidants to release environmentally benign N_2 as the only byproduct. Despite their utility in C-H amination, however, the need for the expensive metal catalysts and precious silver salt to activate metal catalysts are economically and environmentally disadvantageous, especially for future industrial applications. Therefore, the development of a low-cost and efficient metal catalyst as an alternative to pre-activated metal species is highly desired.

Although ruthenium complexes have been extensively used as one of the most effective catalysts for the C-H bond functionalization,⁹ many reported examples are limited to $[(p-cymene)RuCl_2]_2$ -catalyzed system in the presence of silver salt or other additives.¹⁰ RuHCl(CO)(PPh₃)₃, which is readily available from triphenylphosphine, formaldehyde and ruthenium trichloride as raw materials,¹¹ has been used to catalyze hydrogen transfer organic reactions in the past years.¹² Herein, we first describe a readily available RuHCl(CO)(PPh₃)₃-catalyzed direct C-H amidation of arenes without requiring additional silver salt and additive (Scheme 1b).

RESULTS AND DISCUSSION

	0 N-			
		Catalyst (mol%)		I
	Н	solvent, <i>T</i> , 12 h		
	1a 2a	-	3a	
Entry	Catalyst(mol%)	Solv.	T(°C)	Yield (%) ^b
1	RuHCl(CO)(PPh ₃) ₃ (5)	toluene	80	33
2	RuHCl(CO)(PPh ₃) ₃ (5)	THF	80	trace
3	RuHCl(CO)(PPh ₃) ₃ (5)	CH₃CN	80	22
4	RuHCl(CO)(PPh ₃) ₃ (5)	DMSO	80	NR
5	RuHCl(CO)(PPh ₃) ₃ (5)	DMF	80	trace
6	RuHCl(CO)(PPh ₃) ₃ (5)	DCE	80	52
7	RuHCl(CO)(PPh ₃) ₃ (5)	DCE	110	85
8	RuHCl(CO)(PPh ₃) ₃ (5)	DCE	100	88
9	RuHCl(CO)(PPh ₃) ₃ (5)	DCE	90	75
10	RuHCI(CO)(PPh ₃) ₃ (10)	DCE	100	87
11	RuHCl(CO)(PPh ₃) ₃ (3)	DCE	100	69
12 ^c	RuHCl(CO)(PPh ₃) ₃ (5)	DCE	100	79
13 ^d	RuHCl(CO)(PPh ₃) ₃ (5)	DCE	100	86
14	RuCl ₃ (5)	DCE	100	NR
15	Ru ₃ (CO) ₁₂ (5)	DCE	100	NR
16	$RuH_2(CO)(PPh_3)_2(5)$	DCE	100	NR
17	RuH ₂ (PPh ₃) ₄ (5)	DCE	100	NR
18	[RuCl ₂ (p-cymene)] ₂ (5)	DCE	100	trace
19	Cul	DCE	100	NR
20	Pd(OAc) ₂	DCE	100	NR
^a Unless phenylp (0.24 m tempera chromat	otherwise noted, all the reac yridine (1a) (0.20 mmol) an mol) with metal catalysts ture for 12 h under Ar in a s tography on SiO ₂ . ^b Isolated yi	tions were car d 4-methylben in solvent (1 ealed reaction eld. ^c The react	ried out firstly zenesulfonyl a .0 mL) at the tube, followed ion time was 8	using 2 izide(2a setting by flasi 3 h. ^d Th

Our initial investigation was carried out by using 2-phenylpyridine (**1a**) as the model substrate and *p*-toluenesulfonyl azide(**2a**) as nitrogen sources (Table 1). To our delight, the amination reaction catalyzed by RuHCl(CO)(PPh₃)₃ in toluene at 80 $^{\circ}$ C afforded the designed 4-methyl-*N*-[2-(pyridin-2-yl)phenyl]-benzenesulfonamide (**3a**) in 33% yield after 12 h (entry 1). Although the conversion

efficiency of **1a** was very low, this positive result greatly encouraged us to continue to evaluate various solvents such as 1,2-DCE, CH₃CN, DMSO, and THF etc, for improving the C-H bond amidation yield (compare entries 1-6). The corresponding solvent screening indicated that 1,2-DCE could serve as the most efficient solvent for this transformation. Gratifyingly, a further significant improvement of the reaction (88% yield) was achieved by increasing reaction temperature to 100 $^{\circ}$ C (entries 6-9). It is noteworthy that the amidation took place even with lower catalyst loading albeit with slightly lower yield (69% yield) under the present catalyst system (entry 11). The reaction time was extended to 24 hours or shortened to 8 hours, and the yield was slightly reduced(entries 12-13). Investigations on other catalysts in this reaction indicated that RuHCl(CO)(PPh₃)₃ displayed a significant catalytic activity while other catalysts have no effect (entries 14-20).





^aUnless otherwise noted, all the reactions were carried out firstly using arene (1) (0.20 mmol) and azide(**2a**) (0.24 mmol) with RuHCl(CO)(PPh₃)₃ (5 mol%) in DCE (1.0 mL) at the 100°C for 12 h under Ar in a sealed reaction tube, followed by flash chromatography on SiO₂. ^{*b*}Isolated yield. ^cThe reaction time was 24 h.

With the optimized conditions for the RuHCl(CO)(PPh₃)₃-catalyzed arene C–H bond amidation established, we next investigated the scope of the current procedure by testing various arenes in the reaction with *p*-toluenesulfonyl azide(**2a**). Electronic variation of *para*-substituents did not much influence the reaction efficiency (**3a-3h**). The amidation conditions were compatible with various functional groups such as fluoro, chloro, methyl, methoxy, phenyl and acetyl. Substrates bearing electron-withdrawing groups such as trifluoromethyl (**3e**) underwent the amidation in high yield of 82%. In addition, the amidation was highly regioselective as proved in the reaction of meta-

substituted arene (**3i** and **3j**, respectively). Moreover, a variation of the substitution pattern on the pyridine moiety proved to be well tolerated with this transformation (**3k-3l**). The reactivity for some other directing groups was briefly investigated under the current ruthenium system (Scheme 2). We were pleased to observe that representative directing groups, such as pyrimidine(**3m**), pyrazole (**3n-3o**), azo(3p), amide(3q), and *N*-phenyl-pyrrolidone(3r-3s) moieties all facilitated the desired amidation. Commercially available benzo[h]quinoline successfully underwent amination to give**3t**and the structure of**3t**was unambiguously characterized by X-raycrystallographic analysis.

The scope of sulfonyl azides was then examined in the amidation of 2-phenylpyridine (**1a**). Arenesulfonyl azide substrates substituted with methoxy (**4a**), bromo (**4c**), chloro (**4d**), nitro (**4e**), acetamido (**4f**) or trifluoromethyl (**4g**) groups were readily amidated at the orthoposition of 2-phenylpyridine (Scheme 3). Of note, introducing one or more methyl group to ortho- and meta-position of the phenyl ring could still lead to good yields of **4h**, **4i** and **4j** (62–75%) regardless of the steric hindrance. Moreover, heteroarylsulfonyl azides, 1-naphthylsulfonyl azides and alkylsulfonyl azides were also allowed for this transformation and produced the corresponding sulfonylamidation products **4k–4n** in 79-86% yields. Since the reaction temperature is relatively high, when benzoyl azide was used as azide source, Curtius rearrangement reaction was observed and the selective C–C amidation products was obtained mainly (**4o**). According to the reports of Chang, C–N amidation products^{3h} were obtained using[IrCpCl₂]₂ as catalyst at room-temperature and C–C Amidation products^{7g} were obtained using [RhCpCl₂]₂ as catalyst at 70°C.

Scheme 3. Substrate Scope of azide *a*, *b*



^aUnless otherwise noted, all the reactions were carried out firstly using arene (**1a**) (0.20 mmol) and azide(**2**) (0.24 mmol) with RuHCl(CO)(PPh₃)₃ (5 mol%) in DCE (1.0 mL) at the 100°C for 12 h under Ar in a sealed reaction tube, followed by flash chromatography on SiO₂. ^{*b*}Isolated vield.

The corresponding synthetic application of RuHCl(CO)(PPh₃)₃-catalyzed direct amidation is shown in Scheme 4. N-(2-(benzo[d]oxazol-2-yl)phenyl)-4-methylbenzenesulfonamide(**6a**) can undergo excited-state intramolecular proton transfer (ESIPT) upon excitation.¹³ The zinc chelate complexes of **6a** was used as lectroluminescent materials for organic light-emitting diodes.¹⁴ Using our reaction conditions, compound **6a** can be obtained at a yield of 88% (eq 1 in Scheme 4). In order to investigate the reactivity of RuHCl(CO)(PPh₃)₃ catalyst for aliphatic substrate, We used *N*-propylpicolinamide(**7a**) as the substrate to react under standard conditions(eq 2 in Scheme 4). Unfortunately, no target product was found in the reaction.



To gain a mechanistic insight into the RuHCl(CO)(PPh₃)₃-catalyzed amidation reaction, a series of preliminary studies were carried out. When biphenyl(**1aa**) was uesd to replace 2-phenylpyridine(**1a**) in standard reaction condition, we found that there was no C–H bond amidation product (eq 1 in Scheme 5). The H/D exchange of 2-pyridylbenzene (**1a**) was conducted in RuHCl(CO)(PPh₃)₃/CH₃OD system for 12 h in the absence of azide, and 48% deuterium incorporation at the arene C2-position was observed (eq 2 in Scheme 5). This result implied that amido moiety played a key role of chelation in promoting the arene C2-H bond cleavage. Subsequently, the parallel kinetic experiments from **1a** and *d*-**1a** ($k_{\rm H}/k_{\rm D} = 1.8$) further indicated that the aryl C-H bond-breaking just influenced, but did not solely dominate the reaction rate (eq 3 in Scheme 5) (see SI for more details).



Based on the above research data and previous reports, a plausible mechanistic pathway is displayed in Scheme 6 with 2-pyridylbenzene(**1a**) and *p*-toluenesulfonyl azide(**2a**) as model substrate. The C-H bond activation is supposed to proceed by an electrophilic aromatic metalation pathway, leading to the five-menbered ruthenacycle intermediate **I**. Then, a reversible coordination of azide to the Ru(II) center produces intermediate **II**. The sulfonamido moiety of intermediate **II** subsequently insert into the Ru-C bond directly by releasing a nitrogen molecule to deliver intermediate **III**. which is eventually protonated to afford the target amidated products.



CONCLUSION

In conclusion, we have first presented direct sp² C-H amidation of arenes with azides as the nitrogen source using a new and inexpensive $RuHCl(CO)(PPh_3)_3$ catalysis. This protocol does not require silver salt and other additives, and shows wide substrate scope and functional group tolerance. Further investigation of the mechanism and applications of this catalyst system are ongoing.

EXPERIMENTAL SECTION

General Methods: All reactions were carried out in flame-dried sealed tubes with magnetic stirring. Unless otherwise noted, all experiments were performed under argon atmosphere. All reagents were purchased from TCI, Acros or Strem. Solvents were treated with 4 Å molecular sieves or sodium and distilled prior to use. RuHCl(CO)(PPh₃)₃ was prepared according to the previously reported procedures¹¹. The starting materials 2-phenylpyridine substrates **1a-11**,¹⁵ various directing groups substrates **1m-1s**,¹⁶ **5a**,¹⁷ **7a**,¹⁸ sulfonyl azides **2a-2o**¹⁹ and benzoyl azide **2p**¹⁹were prepared according to the previously reported procedures. Purifications of reaction products were carried out by flash chromatography using Qingdao Haiyang Chemical Co. Ltd silica gel (200-300 mesh). Infrared spectra (IR) were recorded on a Brucker TENSOR 27 FTIR spectrophotometer and are reported as wavelength numbers (cm⁻¹). Infrared spectra were recorded by preparing a KBr pellet containing the title compound. ¹H NMR and ¹³C NMR spectra were recorded with tetramethylsilane (TMS) as internal standard at ambient temperature unless otherwise indicated on a Brucker DPX 600 fourier Transform

spectrometer operating at 400 MHz for ¹H NMR and 100 MHz for ¹³C NMR. Chemical shifts are reported in parts per million (ppm) and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), broad singlet (bs), doublet (d), triplet (t). Splitting patterns that could not be interpreted or easily visualized are designated as multiple (m). Low resolution mass spectra were recorded using a Waters HPLC/ZQ4000 Mass Spectrometer. High resolution mass spectra (HRMS) were recorded on an IF-TOF spectrometer (Micromass). Gas chromatograph mass spectra were obtained with a SHIMADZU model GCMS-QP5000 spectrometer. Crystal data were collected on a Bruker D8 Advance employing graphite monochromated Mo - K α radiation (λ = 0.71073 Å) at 295 (2) K and operating in the φ - ω scan mode. The structure was solved by direct methods SHELXS-97.

Typical Procedure for the amidation of of arenes with azides (3a–3t, 4a-4o, 6a): All of the products (3a–3t, 4a-4o, 6a) were obtained according to the following procedure. To a screw capped vial with a spinvane triangular-shaped Teflon stir bar were added arene (1, 0.2 mmol), azide (2, 0.24 mmol), RuHCl(CO)(PPh₃)₃ (9.5 mg, 0.01 mmol, 5 mol %) and 1, 2-dichloroethane (1.0 mL) under Ar atmosphere conditions. The reaction mixture was stirred at 100 °C for 12 h, filtered through a pad of celite and then washed with ethyl acetate (10 mL × 3). Organic solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel with ethyl acetate/petroleum as the eluent to give the desired products. All of the yields are isolated yield.

4-Methyl-*N*-(**2-(pyridin-2-yl)phenyl)benzenesulfonamide (3a)**²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 57.0 mg, 88% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.16 (s, 1H), 8.60 – 8.54 (m, 1H), 7.69 (dt, *J* = 6.9, 2.1 Hz, 2H), 7.51 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.40 – 7.30 (m, 4H), 7.25 – 7.20 (m, 1H), 7.17 – 7.12 (m, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 2.25 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.0, 147.3, 143.0, 137.5, 136.8, 136.4, 130.1, 129.1, 128.5, 127.5, 126.7, 124.7, 123.4, 122.3, 122.1, 21.4. HRMS (ESI): Exact mass calcd for C₁₈H₁₇N₂O₂S [M+H]⁺ 325.1005, Found 325.1007.

4-Methyl-*N***-(5-methyl-2-(pyridin-2-yl)phenyl)benzenesulfonamide** (3b)²¹: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 57.6 mg, 85% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.25 (s, 1H), 8.54 (d, *J* = 4.4 Hz, 1H), 7.65 (td, *J* = 7.9, 1.7 Hz, 1H), 7.51 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 3H), 7.18 (dd, *J* = 7.2, 5.1 Hz, 1H), 6.94 (d, *J* = 8.1 Hz, 3H), 2.34 (s, 3H), 2.24 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.1, 147.2, 142.9, 140.5, 137.4, 136.7, 136.4, 129.1, 128.3, 126.7, 125.6, 124.7, 123.8, 121.9, 121.8, 21.4, 21.4. HRMS (ESI): Exact mass calcd for C₁₉H₁₉N₂O₂S [M+H]⁺ 339.1162, Found 339.1162.

N-(5-methoxy-2-(pyridin-2-yl)phenyl)-4-methylbenzenesulfonamide (3c)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a light yellow solid, 55.2 mg, 78% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.83 (s, 1H), 8.54 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.67 (td, *J* = 8.1, 1.8 Hz, 1H), 7.47 (dd, *J* = 8.4, 7.1 Hz, 3H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.24 (d, *J* = 2.6 Hz, 1H), 7.17 (ddd, *J* = 7.4, 5.0, 0.8 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.64 (dd, *J* = 8.8, 2.6 Hz, 1H), 3.80 (s, 3H), 2.26 (s, 3H). ¹³C {¹H}NMR (100 MHz, CDCl₃) δ 160.9, 157.0, 147.0, 143.1, 138.8, 137.5, 136.6, 129.5, 129.2, 126.9, 121.3, 121.3, 119.0, 110.8, 106.9, 55.4, 21.4. HRMS (ESI): Exact mass calcd for C₁₉H₁₉N₂O₃S [M+H]⁺ 355.1111, Found 355.1112.

N-(5-chloro-2-(pyridin-2-yl)phenyl)-4-methylbenzenesulfonamide (3d)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 60.3 mg, 84% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.53 (s, 1H), 8.60 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.50 – 7.42 (m, 4H), 7.27 (ddd, *J* = 7.5, 4.7, 0.8 Hz, 1H), 7.09 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 2H), 2.29 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.2, 147.3, 143.4, 138.3, 137.7, 136.3, 135.9, 129.4, 129.3, 126.8, 124.8, 124.4, 122.4, 122.3, 122.0, 21.4. HRMS (ESI): Exact mass calcd for C₁₈H₁₆ClN₂O₂S [M+H]⁺ 359.0616, Found 359.0618.

4-Methyl-*N*-(**2-**(**pyridin-2-yl**)-**5-**(**trifluoromethyl**)**phenyl**)**benzenesulfonamide**(**3e**)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 64.3 mg, 82% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.40 (s, 1H), 8.65 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.98 (d, *J* = 0.7 Hz, 1H), 7.79 (td, *J* = 7.9, 1.8 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.30 (m, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 2.28 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 155.8, 147.6, 143.5, 137.9, 137.6, 136.1, 131.9(q, J = 32.8 Hz), 129.4, 129.0, 126.8, 123.4 (q, J = 271.9 Hz), 123.0, 122.6, 120.8(q, J = 4.0 Hz), 119.5(q, J = 4.0 Hz), 21.4. ¹⁹F NMR (376 MHz, CDCl₃) δ -63.01.HRMS (ESI): Exact mass calcd for C₁₉H₁₆F₃N₂O₂S [M+H]⁺ 393.0879, Found 393.0878.

N-(5-acetyl-2-(pyridin-2-yl)phenyl)-4-methylbenzenesulfonamide(3f)²¹: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a light yellow solid, 58.6 mg, 80% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.24 (s, 1H), 8.65 (d, *J* = 4.1 Hz, 1H), 8.24 (d, *J* = 1.5 Hz, 1H), 7.76 (ddd, *J* = 16.5, 8.2, 1.7 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.32 (dd, *J* = 7.2, 5.2 Hz, 1H), 7.00 (d, *J* = 8.1 Hz, 2H), 2.62 (s, 3H), 2.28 (s, 3H). ¹³C {¹H}NMR (100 MHz, CDCl₃) δ 197.2, 156.0, 147.6, 143.4, 138.0, 137.7, 137.3, 136.2, 130.8, 129.3, 128.7, 126.8, 123.6, 123.3, 122.9, 122.7, 26.8, 21.4. HRMS (ESI): Exact mass calcd for C₂₀H₁₉N₂O₃S [M+H]⁺ 367.1111, Found 367.1109.

N-(5-fluoro-2-(pyridin-2-yl)phenyl)-4-methylbenzenesulfonamide(3g)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 57.4 mg, 84% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.78 (s, 1H), 8.59 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.74 (td, *J* = 8.0, 1.8 Hz, 1H), 7.55 (dd, *J* = 8.8, 6.1 Hz, 1H), 7.52 – 7.38 (m, 4H), 7.25 (dd, *J* = 7.0, 5.1 Hz, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 6.85 – 6.74 (m, 1H), 2.28 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 163.3(d, *J* = 248.0 Hz), 156.3, 147.2, 143.4, 139.1(d, *J* = 11.0 Hz), 137.8, 136.4, 130.0(d, *J* = 9.0 Hz), 129.4, 126.8, 122.3(d, *J* = 4.0 Hz), 122.1, 121.9, 111.2(d, *J* = 22.0 Hz), 109.0(d, *J* = 26.0 Hz), 21.4. HRMS (ESI): Exact mass calcd for C₁₈H₁₆FN₂O₂S [M+H]⁺ 343.0911, Found 343.0909.

4-Methyl-*N*-(**4**-(**pyridin-2-yl**)-[**1,1'-biphenyl**]-**3-yl**)**benzenesulfonamide**(**3h**)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 68.8 mg, 86% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.40 (s, 1H), 8.60 (d, *J* = 4.1 Hz, 1H), 7.97 (d, *J* = 1.7 Hz, 1H), 7.70 (td, *J* = 8.0, 1.8 Hz, 1H), 7.64 – 7.58 (m, 3H), 7.44 (dd, *J* = 12.5, 7.7 Hz, 5H), 7.40 – 7.35 (m, 2H), 7.23 (dd, *J* = 7.4, 5.6 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 2H), 2.25 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.8, 147.4, 143.1, 142.8, 139.6, 137.5, 137.4, 136.5, 129.2, 128.9, 128.8, 128.0, 127.1, 126.9, 125.8, 123.0, 122.1, 121.4, 21.4. HRMS (ESI): Exact mass calcd for C₂₄H₂₁N₂O₂S [M+H]⁺ 401.1318, Found 401.1319.

N-(4-chloro-2-(pyridin-2-yl)phenyl)-4-methylbenzenesulfonamide(3i): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, m.p. 172 - 173 °C. 56.6 mg, 79% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.03 (s, 1H), 8.60 (d, *J* = 4.8 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.7 Hz, 1H), 7.49 (d, *J* = 1.8 Hz, 1H), 7.38 - 7.32 (m, 3H), 7.31 - 7.25 (m, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 2.27 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 155.7, 147.6, 143.2, 137.7, 136.1, 135.4, 130.1, 129.9, 129.3, 128.9, 128.3, 126.7, 124.9, 122.7, 122.3, 21.4. IR (KBr) 3452, 3261, 3088, 2924, 1614, 1508, 1337, 1155, 1091, 814, 737 cm⁻¹.HRMS (ESI): Exact mass calcd for C₁₈H₁₆ClN₂O₂S [M+H]⁺ 359.0616, Found 359.0617.

4-Methyl-*N*-(**4-methyl-2-(pyridin-2-yl)phenyl)benzenesulfonamide**(**3j**)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 55.4 mg, 82% yield. ¹H NMR (400 MHz, CDCl₃) δ 11.79 (s, 1H), 8.57 – 8.51 (m, 1H), 7.65 (td, *J* = 7.9, 1.8 Hz, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.28 (dd, *J* = 16.6, 8.2 Hz, 4H), 7.20 (dd, *J* = 7.3, 5.1 Hz, 1H), 7.14 (dd, *J* = 8.3, 1.5 Hz, 1H), 6.90 (d, *J* = 8.1 Hz, 2H), 2.31 (s, 3H), 2.23 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 157.1, 147.4, 142.8, 137.4, 136.2, 134.7, 134.0, 130.8, 129.1, 129.0, 128.1, 126.6, 124.2, 122.3, 122.0, 21.4, 21.0. HRMS (ESI): Exact mass calcd for C₁₉H₁₉N₂O₂S [M+H]⁺ 339.1162, Found 339.1162.

4-Methyl-*N*-(**2**-(**4-methylpyridin-2-yl)phenyl)benzenesulfonamide**(**3**k)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 50.0 mg, 74% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.33 (s, 1H), 8.41 (d, *J* = 0.7 Hz, 1H), 7.67 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.50 (dd, *J* = 7.9, 1.2 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.35 – 7.26 (m, 2H), 7.11 (td, *J* = 7.8, 1.2 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 2.26 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 154.3, 147.5, 143.0, 138.1, 136.8, 136.6, 131.9, 129.7, 129.1, 128.2, 127.1, 126.8, 124.5, 122.9, 121.7. HRMS (ESI): Exact mass calcd for C₁₉H₁₉N₂O₂S [M+H]⁺ 339.1162, Found 339.1162.

4-Methyl-*N*-(**2**-(**5**-(**trifluoromethyl**)**pyridin-2-yl**)**phenyl**)**benzenesulfonamide**(**3l**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, m.p. 157 - 159 °C. 62.7 mg, 80% yield. ¹H NMR (400 MHz, CDCl₃) δ 11.36 (s, 1H), 8.85 (s, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 2H), 2.28 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 160.4, 144.6(q, J = 4.0 Hz), 143.3, 136.9, 136.2, 134.3(q, J = 3.0 Hz), 131.3, 129.2, 129.0, 126.9, 126.7, 125.2, 124.7, 124.3, 123.5(q, J = 304.0 Hz), 122.3, 21.4. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.45. IR (KBr) 3450, 3358, 3260, 3067, 2931, 2304, 1594, 1415, 1339, 1161, 735, 565cm⁻¹.HRMS (ESI): Exact mass calcd for C₁₉H₁₆F₃N₂O₂S [M+H]⁺ 393.0879, Found 393.0880.

4-Methyl-*N*-(**2-(pyrimidin-2-yl)phenyl)benzenesulfonamide(3m)**²²: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a light yellow solid, 55.3 mg, 85% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.50 (s, 1H), 8.81 (d, J = 4.9 Hz, 2H), 8.47 (dd, J = 8.0, 1.6 Hz, 1H), 7.68 (dd, J = 8.3, 1.0 Hz, 1H), 7.64 – 7.59 (m, 2H), 7.41 – 7.36 (m, 1H), 7.24 (t, J = 4.9 Hz, 1H), 7.14 (ddd, J = 8.4, 7.3, 1.2 Hz, 1H), 7.10 (d, J = 8.0 Hz, 2H), 2.30 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) 13C NMR (101 MHz, CDCl₃) δ 164.4, 156.4, 143.4, 138.8, 136.7, 132.1, 130.6, 129.4, 127.1, 123.6, 120.4, 118.8, 21.5. HRMS (ESI): Exact mass calcd for C₁₇H₁₆N₃O₂S [M+H]⁺ 326.0958, Found 326.0959.

4-Methyl-*N***-(2-(3-methyl-1H-pyrazol-5-yl)phenyl)benzenesulfonamide(3n)**: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a light yellow solid, 43.8 mg, 67% yield. ¹H NMR (400 MHz, CDCl₃) δ 11.63 (s, 1H), 10.65 (s, 1H), 7.68 (d, *J* = 8.3 Hz, 3H), 7.49 (dd, *J* = 7.8, 1.4 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.06 (td, *J* = 7.6, 1.1 Hz, 1H), 6.25 (s, 1H), 2.34 (s, 3H), 2.30 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 151.3, 143.4, 140.1, 136.4, 135.3, 129.4, 128.3, 127.7, 127.2, 123.7, 121.6, 120.1, 102.4, 21.5, 10.7. IR (KBr) 3358, 3260, 3067, 2962, 2872, 1594,1502, 1415, 1339, 1161, 802,742cm⁻¹.HRMS (ESI): Exact mass calcd for C₁₇H₁₈N₃O₂S [M+H]⁺ 328.1114, Found 328.1113.

N-(2-(1H-pyrazol-1-yl)phenyl)-4-methylbenzenesulfonamide(3o)²²: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a light yellow solid, 27.5 mg, 44% yield. ¹H NMR (400 MHz, CDCl₃) δ 10.04 (s, 1H), 7.84 – 7.72 (m, 2H), 7.32 (ddd, *J* = 14.3, 7.3, 2.8 Hz, 4H), 7.25 – 7.14 (m, 2H), 7.05 (d, *J* = 6.5 Hz, 2H), 6.38 (d, *J* = 1.8 Hz, 1H), 2.33 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 143.2, 141.2, 136.1, 131.3, 130.2, 129.3, 128.0, 126.6, 125.8, 125.4, 121.8, 107.2, 21.5. HRMS (ESI): Exact mass calcd for C₁₆H₁₆N₃O₂S [M+H]⁺ 314.0958, Found 314.0960.

4-Methyl-*N*-(**2-(phenyldiazenyl)phenyl)benzenesulfonamide(3p)**²³: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 39.3 mg, 56% yield. ¹H NMR (400 MHz, CDCl₃) δ 9.74 (s, 1H), 7.84 – 7.79 (m, 2H), 7.75 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.67 (d, J = 7.2 Hz, 2H), 7.54 (dd, J = 6.7, 4.5 Hz, 3H), 7.39 (t, J = 7.8 Hz, 1H), 7.15 (dd, J = 17.0, 7.8 Hz, 3H), 2.29 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 152.0, 144.0, 140.0, 136.2, 134.5, 132.5, 131.7, 129.7, 129.3, 127.2, 124.3, 122.8, 122.7, 120.2, 21.5. HRMS (ESI): Exact mass calcd for C₁₉H₁₈N₃O₂S [M+H]⁺ 352.1114, Found 352.1115.

3-(4-Methylphenylsulfonamido)-*N***-propylthiophene-2-carboxamide(3q)**: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a light yellow solid, 52.7 mg, 78% yield. ¹H NMR (400 MHz, CDCl₃) δ 10.63 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.22 (t, *J* = 6.3 Hz, 3H), 5.75 (s, 1H), 3.29 (dd, *J* = 13.6, 6.6 Hz, 2H), 2.36 (s, 3H), 1.56 (dd, *J* = 14.6, 7.3 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 163.7, 143.9, 142.3, 136.6, 129.7, 127.1, 127.0, 121.8, 113.3, 41.4, 22.8, 21.6, 11.3. IR (KBr) 3356, 3264, 3064, 2961, 2926, 2872, 1593, 1415, 1339, 1161, 802 cm⁻¹.HRMS (ESI): Exact mass calcd for C₁₅H₁₉N₂O₃S₂ [M+H]⁺ 339.0832, Found 339.0829.

4-Methyl-*N***-(1-pivaloylindolin-7-yl)benzenesulfonamide(3r)**⁸: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate =4:1, v/v) affords the title compound as a light yellow solid, 61.7mg, 83% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.70 (s, 1H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 6.3 Hz, 3H), 7.09 (d, *J* = 7.3 Hz, 1H), 3.78 (t, *J* = 7.4 Hz, 2H), 2.94 (t, *J* = 7.4 Hz, 2H), 2.35 (s, 3H), 1.22 (s, 9H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 178.0, 143.1, 137.9, 137.5, 134.8, 129.3, 127.0, 126.7, 126.6, 126.2, 122.5, 51.5, 39.9, 30.2, 28.1, 21.4. HRMS (ESI): Exact mass calcd for C₂₀H₂₅N₂O₃S [M+H]⁺ 373.1581, Found 373.1584.

N-(1-benzoylindolin-7-yl)-4-methylbenzenesulfonamide(3s)⁸: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 56.4 mg, 72% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.93 (s, 1H), 7.53 – 7.48 (m, 1H), 7.43 (tt, *J* = 7.3, 3.6 Hz, 5H), 7.30 – 7.27 (m, 2H), 7.18 (dd, *J* = 12.1, 5.2 Hz, 3H), 7.10 (dd, *J* = 7.4, 0.9 Hz, 1H), 3.72

(t, J = 7.7 Hz, 2H), 2.91 (t, J = 7.7 Hz, 2H), 2.45 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 174.2, 169.7, 143.1, 137.9, 136.0, 135.3, 135.0, 131.6, 129.5, 129.4, 128.4, 128.0, 127.1, 126.9, 126.7, 126.4, 122.8, 54.4, 29.5, 21.6. HRMS (ESI): Exact mass calcd for C₂₂H₂₁N₂O₃S [M+H]⁺ 393.1268, Found 393.1264.

N-(**benzo**[*h*]**quinolin-10-yl**)-**4**-ethylbenzenesulfonamide(3t)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 64.0 mg, 92% yield. ¹H NMR (400 MHz, CDCl₃) δ 15.26 (s, 1H), 8.92 (dd, *J* = 4.5, 1.7 Hz, 1H), 8.18 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.94 – 7.85 (m, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.44 (m, 4H), 7.06 (d, *J* = 8.2 Hz, 2H), 2.21 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 147.3, 145.8, 143.2, 138.6, 137.3, 136.7, 135.2, 129.4, 129.0, 128.6, 127.3, 127.2, 125.4, 122.8, 121.2, 117.3, 116.1, 21.4. HRMS (ESI): Exact mass calcd for C₂₀H₁₇N₂O₂S [M+H]⁺ 349.1005, Found 349.1004.

4-Methoxy-*N***-(2-(pyridin-2-yl)phenyl)benzenesulfonamide(4a)**²¹: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a light yellow solid, 46.2 mg, 68% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.06 (s, 1H), 8.61 (d, *J* = 4.8 Hz, 1H), 7.71 (dd, *J* = 12.8, 4.9 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 8.3, 6.5 Hz, 3H), 7.35 (dd, *J* = 11.2, 4.3 Hz, 1H), 7.24 (dd, *J* = 7.8, 5.4 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 8.9 Hz, 2H), 3.74 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 162.6, 157.2, 147.4, 137.5, 136.9, 131.1, 130.1, 128.8, 128.5, 127.6, 124.7, 123.5, 122.3, 122.1, 113.7, 55.5. HRMS (ESI): Exact mass calcd for C₁₈H₁₇N₂O₃S [M+H]⁺ 341.0954, Found 341.0958.

N-(2-(pyridin-2-yl)phenyl)benzenesulfonamide(4b)²⁴: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 52.1 mg, 84% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.22 (s, 1H), 8.62 – 8.51 (m, 1H), 7.74 – 7.64 (m, 2H), 7.50 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.44 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.38 – 7.29 (m, 3H), 7.22 (ddd, *J* = 7.5, 4.9, 0.9 Hz, 1H), 7.19 – 7.11 (m, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.9, 147.3, 139.2, 137.7, 136.6, 132.3, 130.1, 128.6, 127.7, 126.6, 125.0, 123.7, 122.3, 122.2. HRMS (ESI): Exact mass calcd for C₁₇H₁₅N₂O₂S [M+H]⁺ 311.0849, Found 311.0851.

4-Bromo-*N***-(2-(pyridin-2-yl)phenyl)benzenesulfonamide(4c)**²⁴: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 63.8 mg, 82% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.09 (s, 1H), 8.58 (d, *J* = 4.8 Hz, 1H), 7.73 (ddd, *J* = 11.7, 8.8, 5.0 Hz, 2H), 7.53 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.38 (dt, *J* = 9.8, 2.1 Hz, 2H), 7.31 – 7.24 (m, 5H), 7.21 (dd, *J* = 10.9, 4.3 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.9, 147.4, 138.1, 137.7, 136.2, 131.7, 130.3, 128.6, 128.2, 128.1, 127.2, 125.4, 124.3, 122.4, 122.3. HRMS (ESI): Exact mass calcd for C₁₇H₁₄BrN₂O₂S [M+H]⁺ 388.9954, Found 388.9953.

4-Chloro-*N*-(**2-(pyridin-2-yl)phenyl)benzenesulfonamide**(**4d**)²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 59.1 mg, 86% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.15 (s, 1H), 8.62 – 8.54 (m, 1H), 7.75 – 7.68 (m, 2H), 7.53 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.40 – 7.32 (m, 4H), 7.27 – 7.23 (m, 1H), 7.22 – 7.17 (m, 1H), 7.14 – 7.06 (m, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.8, 147.4, 138.7, 137.7, 137.6, 136.3, 130.3, 128.7, 128.6, 128.1, 128.0, 125.4, 124.1, 122.4, 122.3.HRMS (ESI): Exact mass calcd for C₁₇H₁₄ClN₂O₂S [M+H]⁺ 345.0459, Found 345.0458.

4-Nitro-*N***-(2-(pyridin-2-yl)phenyl)benzenesulfonamide(4e)**²⁰: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 55.4mg, 78% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.44 (s, 1H), 8.61 (dd, *J* = 4.9, 0.9 Hz, 1H), 8.01 – 7.95 (m, 2H), 7.72 (ddd, *J* = 12.1, 6.6, 3.5 Hz, 2H), 7.65 – 7.60 (m, 2H), 7.56 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.40 (ddd, *J* = 9.9, 6.5, 2.0 Hz, 2H), 7.31 – 7.23 (m, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.7, 149.7, 147.4, 144.9, 137.9, 135.8, 130.5, 128.6, 127.9, 127.7, 125.7, 124.1, 123.6, 122.5, 122.2. HRMS (ESI): Exact mass calcd for C₁₇H₁₄N₃O₄S [M+H]⁺ 356.0700, Found 356.0698.

N-(4-(*N*-(2-(pyridin-2-yl)phenyl)sulfamoyl)phenyl)acetamide(4f): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 2:1, v/v) affords the title compound as a light yellow solid, 59.4 mg, 81% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.56 – 8.52 (m, 1H), 7.95 (s, 1H), 7.70 (td, J = 7.9, 1.8 Hz, 1H), 7.63 (d, J = 8.1 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.34 (s, 4H), 7.33 – 7.28 (m, 1H), 7.22 (dd, J = 7.2, 5.2 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 2.13 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 169.0, 156.9, 147.2, 142.0, 137.9, 136.5, 133.5, 130.2, 128.6, 127.8, 127.6, 125.0, 123.4, 122.4, 122.3, 118.9, 24.6. HRMS (ESI): Exact mass calcd for C₁₉H₁₈N₃O₃S [M+H]⁺ 368.1064, Found 368.1064.

N-(2-(pyridin-2-yl)phenyl)-4-(trifluoromethyl)benzenesulfonamide(4g)²¹: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 67.3 mg, 89% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.12 (s, 1H), 8.59 (d, *J* = 4.8 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.68 (dd, *J* = 11.5, 4.2 Hz, 1H), 7.57 – 7.48 (m, 3H), 7.42 (dd, *J* = 13.2, 8.0 Hz, 3H), 7.33 – 7.22 (m, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 156.7, 147.4, 142.4, 137.8, 135.9, 133.8(d, J = 33.0 Hz), 130.3, 128.6, 128.4, 127.1, 125.7, 125.5(q, J = 4.0 Hz), 124.8, 123.2(d, J = 270.0 Hz), 122.3, 122.3. ¹⁹F NMR (376 MHz, CDCl₃) δ -63.19. HRMS (ESI): Exact mass calcd for C₁₈H₁₄F₃N₂O₂S [M+H]⁺ 379.0723, Found 379.0724.

3-Methyl-*N***-**(**2-(pyridin-2-yl)phenyl)benzenesulfonamide(4h**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, m.p. 142 - 143 °C. 48.6 mg, 75% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.08 (s, 1H), 8.61 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.74 - 7.66 (m, 2H), 7.51 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.36 (ddd, *J* = 12.2, 6.6, 2.4 Hz, 2H), 7.27 - 7.22 (m, 3H), 7.15 (ddd, *J* = 10.8, 8.7, 4.4 Hz, 2H), 7.07 - 7.01 (m, 1H), 2.15 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.1, 147.4, 139.1, 138.7, 137.6, 136.7, 133.0, 130.1, 128.5, 128.3, 127.9, 127.0, 124.9, 123.9, 123.8, 122.3, 122.0, 21.1. IR (KBr) 3450, 3063, 2923, 1919, 1590, 1339, 1160, 1092, 724, 656 cm⁻¹.HRMS (ESI): Exact mass calcd for C₁₈H₁₇N₂O₂S [M+H]⁺ 325.1005, Found 325.1008.

2-Methyl-*N*-(**2-(pyridin-2-yl)phenyl)benzenesulfonamide**(**4i**)²⁴: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 43.4mg, 67% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.68 (s, 1H), 8.62 (dd, *J* = 4.1, 0.8 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.78 (td, *J* = 7.9, 1.8 Hz, 1H), 7.65 – 7.55 (m, 3H), 7.33 – 7.23 (m, 3H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.13 – 7.05 (m, 2H), 2.44 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.3, 147.2, 137.9, 137.8, 137.3, 137.1, 132.6, 132.4, 130.2, 129.7, 128.6, 125.9, 125.3, 123.5, 122.1, 122.1, 120.4, 20.0. HRMS (ESI): Exact mass calcd for C₁₈H₁₇N₂O₂S [M+H]⁺ 325.1005, Found 325.1006.

2,3,5,6-Tetramethyl-*N*-(**2-(pyridin-2-yl)phenyl)benzenesulfonamide(4j**): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, m.p. 159 - 161 °C. 45.5 mg, 62% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.39 (s, 1H), 8.62 (d, *J* = 4.3 Hz, 1H), 7.80 - 7.74 (m, 1H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.26 (d, *J* = 5.2 Hz, 1H), 7.24 - 7.20 (m, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.03 (s, 1H), 2.45 (s, 6H), 2.17 (s, 6H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.4, 147.3, 138.4, 137.7, 137.3, 135.7, 135.1, 130.0, 128.7, 125.6, 123.3, 122.0, 121.9, 120.5, 21.0, 17.8. IR (KBr) 3449, 3260, 3085, 3069, 2924, 1604, 1339, 1092, 814, 737 cm⁻¹. HRMS (ESI): Exact mass calcd for C₂₁H₂₃N₂O₂S [M+H]⁺ 367.1475, Found 367.1478.

N-(2-(pyridin-2-yl)phenyl)thiophene-2-sulfonamide(4k): Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, m.p. 140 - 142°C. 53.1mg, 84% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.44 (s, 1H), 8.57 (dd, *J* = 4.0, 0.8 Hz, 1H), 7.80 - 7.69 (m, 2H), 7.57 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.41 - 7.35 (m, 1H), 7.29 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.27 - 7.17 (m, 2H), 7.13 (dd, *J* = 3.6, 0.9 Hz, 1H), 6.75 (dd, *J* = 4.9, 3.9 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.9, 147.4, 140.0, 137.8, 136.5, 131.8, 131.7, 130.2, 128.6, 127.9, 126.9, 125.3, 123.9, 122.3. IR (KBr) 3451, 3266, 3065, 1610, 1508, 1337, 1161, 1081, 814, 737 cm⁻¹.HRMS (ESI): Exact mass calcd for C₁₅H₁₃N₂O₂S₂ [M+H]⁺ 317.0413, Found 317.0412.

N-(2-(pyridin-2-yl)phenyl)naphthalene-1-sulfonamide(4l)²⁵: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 62.1 mg, 86% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.20 (s, 1H), 8.63 (d, *J* = 4.2 Hz, 1H), 8.07 (s, 1H), 7.78 (t, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.62 – 7.55 (m, 2H), 7.44 (dddd, *J* = 19.0, 15.6, 8.4, 1.2 Hz, 5H), 7.22 – 7.12 (m, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.9, 147.3, 137.4, 136.6, 136.3, 134.6, 131.9, 130.2, 129.1, 128.6, 128.5, 128.5, 128.1, 127.9, 127.7, 127.1, 125.0, 123.9, 122.2, 122.1, 122.0. HRMS (ESI): Exact mass calcd for C₂₁H₁₇N₂O₂S [M+H]⁺ 361.1005, Found 361.1007.

N-(2-(pyridin-2-yl)phenyl)methanesulfonamide(4m)²⁴: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 39.2 mg, 79% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.35 (s, 1H), 8.63 (d, *J* = 4.8 Hz, 1H), 7.92 – 7.81 (m, 2H), 7.80 – 7.70 (m, 2H), 7.45 – 7.38 (m, 1H), 7.34 – 7.28 (m, 1H), 7.25 – 7.18 (m, 1H), 2.87 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.2, 147.5, 138.0, 137.5, 130.6, 128.9, 125.5, 124.1, 122.3, 122.2, 120.9, 39.5. HRMS (ESI): Exact mass calcd for C₁₂H₁₃N₂O₂S [M+H]⁺ 249.0692, Found 249.0693.

1-Phenyl-*N***-(2-(pyridin-2-yl)phenyl)methanesulfonamide(4n)**²¹: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 53.8 mg, 83% yield. ¹H NMR (400 MHz, CDCl₃) δ 12.67 (s, 1H), 8.24 (d, *J* = 4.9 Hz, 1H), 7.86 (d, *J* = 8.3 Hz, 1H), 7.83 – 7.74 (m, 3H), 7.42 – 7.35 (m, 1H), 7.21 – 7.14 (m, 2H), 7.11 – 6.97 (m, 5H), 4.27 (s, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.0, 146.9, 138.1, 137.6, 130.6, 130.5, 128.6, 128.3, 124.3, 123.6, 122.0, 121.7, 119.9, 57.5. HRMS (ESI): Exact mass calcd for C₁₈H₁₇N₂O₂S [M+H]⁺ 325.1005, Found 325.1006.

N-phenyl-2-(pyridin-2-yl)benzamide (40)²⁶: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 4:1, v/v) affords the title compound as a light yellow solid, 44.9 mg, 82% yield. ¹H NMR (400 MHz, CDCl₃) δ 9.07 (s, 1H), 8.54 (d, *J* = 4.5 Hz, 1H), 7.68 (dd, *J* = 10.4, 4.4 Hz, 2H), 7.51 - 7.36 (m, 6H), 7.21 (dd, *J* = 14.2, 6.5 Hz, 3H), 7.03 (t, *J* = 7.4 Hz, 1H). ¹³C{¹H} NMR (100

MHz, CDCl₃) δ 167.8, 158.3, 148.7, 138.4, 138.3, 137.0, 136.3, 130.3, 130.2, 129.2, 128.8, 128.7, 124.2, 122.6, 120.1. HRMS (ESI): Exact mass calcd for C₁₈H₁₅N₂O [M+H]⁺ 275.1179, Found 275.1181.

N-(2-(benzo[d]oxazol-2-yl)phenyl)-4-methylbenzenesulfonamide(6a)²⁷: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a light yellow solid, 64.2 mg, 88% yield. ¹H NMR (400 MHz, CDCl₃) δ 11.74 (s, 1H), 8.06 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.84 – 7.72 (m, 4H), 7.57 – 7.51 (m, 1H), 7.43 – 7.34 (m, 3H), 7.10 (dd, *J* = 11.3, 4.5 Hz, 3H), 2.26 (s, 3H). ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 161.4, 149.2, 143.8, 140.5, 138.1, 136.6, 132.6, 129.6, 128.6, 127.3, 125.9, 125.1, 123.2, 120.0, 118.9, 113.6, 110.6, 21.5. HRMS (ESI): Exact mass calcd for C₂₀H₁₇N₂O₃S [M+H]⁺ 365.0955, Found 365.0954.

Control Experiments for the Mechanism Studies

(a) Procedure for the amidation of 1,1'-biphenyl with sulfonyl azides: To a screw capped vial with a spinvane triangular-shaped Teflon stir bar were added 1,1'-biphenyl (1aa, 0.2 mmol), azide (2a, 0.24 mmol), RuHCl(CO)(PPh₃)₃ (9.5 mg, 0.01 mmol, 5 mol %) and 1, 2-dichloroethane (1.0 mL) under Ar atmosphere conditions. The reaction mixture was stirred at 100 °C for 12 h. The reaction mixture was detected by TLC and no new spot was found.

(b) H/D Exchange of 2-phenylpyridine (1a): To a screw capped vial with a spinvane triangular-shaped Teflon stir bar were added 2-phenylpyridine (1a, 0.2 mmol), CD₃OD (2.0 equiv), RuHCl(CO)(PPh₃)₃ (9.5 mg, 0.01 mmol, 5 mol %) and 1,2-dichloroethane (1.0 mL) under Ar atmosphere conditions. The reaction mixture was stirred at 100 °C for 12 h, filtered through a pad of celite and then washed with ethyl acetate (10 mL \times 3). Organic solvents were removed under reduced pressure and the residue was purified by flash chromatography on silical gel(petroleum ether/ ethyl acetate = 9:1, v/v) to afford the desired compound *d*-1a (95% yield) as white oil. The deuterium incorporation was determined to be 48% by ¹H NMR method(see Figure S1). ¹H NMR (400MHz, CDCl3) δ 8.69 (d, J = 4.3 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1.04H), 7.72 (d, J = 5.5 Hz, 2H), 7.46 (s, 2H), 7.43 – 7.38 (m, 1H), 7.21 (t, J = 5.4 Hz, 1H).

(c) Procedure for the preparation of *d*-1a: *d*-1a was synthesized according to the reported procedures.²⁶ In an oven dried schlenk tube, the [RhCp*Cl₂]₂ (10 mol %), 2-phenylpyridine 1a (1 mmol) were taken and then D₂O (3 mL) was added. The reaction mixture was stirred on a preheated oil bath at 110 °C for 6 h. The reaction mixture was cooled to room temperature and diluted with DCM (10 mL) and organic layer was separated. The aqueous layer was extracted twice with DCM (10 mL). The combined organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. The crude so obtained was purified by silica gel column chromatography using petroleum ether (PE) and ethyl acetate (EA) 9:1 as eluent. Yield 117.5 mg, 75% (97% deuterated). ¹H NMR (400 MHz, CDCl3) δ 8.73 (d, J = 4.8 Hz, 1H), 8.03 (d, J = 7.5 Hz, 0.06H),7.78-7.73 (m, 2H), 7.51 (d, J = 7.2 Hz, 2H), 7.46 (dd, J = 8.0, 6.6 Hz, 1H), 7.24 (td, J = 5.0, 3.3 Hz, 1H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 157.4, 149.7, 139.3, 136.8, 129.0, 128.8, 128.7, 126.6(t, J = 24.2 Hz), 122.1, 120.6.

(d) Kinetic isotope effect for this transformation: A 10 mL of reaction tube was charged with 2-phenylpyridine (1a: 62.0 mg, 0.4 mmol; or *d*-1a: 62.8 mg, 0.4mmol), RuHCl(CO)(PPh₃)₃ (19.4 mg, 5 mol%) and DCE (2.0 mL) under Ar. Azide compound 2a (94.6 mg, 0.48 mmol) in DCE (0.5 mL) was then added in one-pot under Ar and the mixture was stirred at 100 °C. Aliquots (0.4 mL) were extracted at 20 minutes intervals for the first 80 min of the reaction. After the solvent of each aliquot (0.4 mL) was removed under reduced pressure

conditions and analyzed by ¹H NMR spectrum(see Figure S2 and Figure S3). A sample plot of the initial rate data for the reaction of both 1a and d-1a was shown in Figure S-4. The above-mentioned data indicated that the KIE from parallel experiments in the early stage (0-80 minutes) is 1.8.

d-3a: Purification by column chromatography on silica gel (petroleum ether/ ethyl acetate = 3:1, v/v) affords the title compound as a light yellow solid; ¹H NMR (400 MHz, CDCl₃) δ 12.23 (s, 1H), 8.58 – 8.48 (m, 1H), 7.73 – 7.61 (m, 2H), 7.50 (d, *J* = 7.8 Hz, 0.23H), 7.38 – 7.27 (m, 4H), 7.22 (dd, *J* = 7.4, 5.0 Hz, 1H), 7.13 (dd, *J* = 6.9, 4.2 Hz, 1H), 6.92 (d, *J* = 8.1 Hz, 2H), 2.22 (s, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃) δ 156.9, 147.3, 143.1, 137.6, 136.7, 136.2, 130.1, 129.2, 128.6, 127.5, 126.7, 124.9, 124.8, 123.5, 123.4, 122.3, 122.2, 21.4. HR-MS (ESI) calcd for [M + H]⁺: C₁₈H₁₆DN₂O₂S: 326.1068, found: 326.1070.

ASSOCIATED CONTENT

Supporting Information

NMR spectra for all isolated compounds, crystallographic data for **3t** (CIF). This material is available free of charge *via* the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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