

Lewis Base Promoted, Direct 1,4-Conjugate Addition to Quinone Imine Ketals: Efficient Access to Unsymmetrical Diaryl Sulfones

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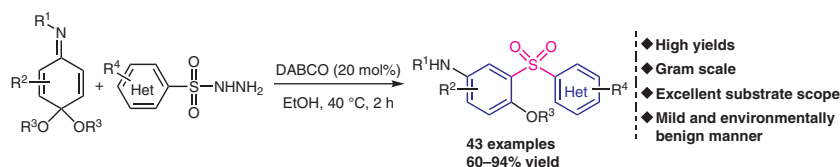
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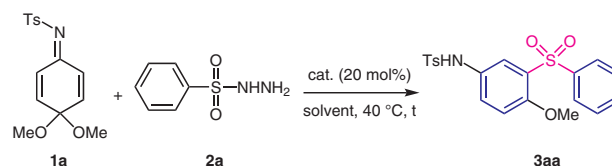
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Abstract An alternative approach with eco-friendliness and high efficiency for the preparation of unsymmetrical diaryl sulfones has been developed. The strategy takes advantage of the reaction of sulfonyl hydrazides with quinone imine ketals catalyzed by DABCO (triethylenediamine) in ethanol. This transformation proceeds *via* a Lewis base promoted, direct 1,4-conjugate addition/sulfonylation/alcohol elimination reaction sequence. The protocol provides an efficient approach to access an array of diverse unsymmetrical diaryl and heterodiaryl sulfones, aryl alkyl sulfones and aryl vinyl sulfones in good to excellent yields.

Key words unsymmetrical diaryl sulfones, eco-friendliness, Lewis base, 1,4-conjugate addition, quinone imine ketals

Unsymmetrical diaryl sulfones are one of the most important sulfur-containing compound classes, playing an important role in organic chemistry, both as common structural elements of bioactive molecules¹ and as versatile intermediates in organic transformations.² In the past few years, many great achievements to construct unsymmetrical diaryl sulfones have been made. Among those achievements, thiols,³ thioethers,⁴ sulfides and sulfoxides,⁵ sulfinic acids and their salts,⁶ sulfonyl chlorides⁷ and DABSO (DABCO·2SO₂)⁸ were frequently used as precursors of the sulfone skeleton. The general methods to access unsymmetrical diaryl sulfones mainly rely on: (i) oxidation of the corresponding sulfides or sulfoxides,^{3–5} or (ii) Lewis acid catalyzed cross-coupling reactions, which include transition-metal-catalyzed cross-coupling reactions^{7d,9} and light-driven transition-metal-catalyzed or photoredox/nickel dual-catalyzed processes^{3a,10} (Scheme 1, A, i and ii). In 1992, Avdeenko and Evgrafova¹¹ described a method using

Table 1 Optimization of the Reaction Conditions^a



| Entry | Catalyst ^b | Solvent | Time (h) | Yield ^c (%) |
|-----------------|---------------------------------|-------------------|----------|------------------------|
| 1 | HOAc | EtOH | 2 | – |
| 2 | PhCO ₂ H | EtOH | 2 | – |
| 3 | Et ₃ N | EtOH | 4 | 65 |
| 4 | DBU | EtOH | 2 | – |
| 5 | DABCO | EtOH | 2 | 85 |
| 6 | DMAP | EtOH | 2 | – |
| 7 | Cs ₂ CO ₃ | EtOH | 2 | – |
| 8 | DABCO | MeOH | 2 | 80 |
| 9 | DABCO | toluene | 2 | 72 |
| 10 | DABCO | CHCl ₃ | 2 | 65 |
| 11 | DABCO | THF | 2 | 60 |
| 12 | DABCO | MeCN | 2 | 50 |
| 13 | DABCO | EtOAc | 2 | 60 |
| 14 | DABCO | H ₂ O | 2 | 40 |
| 15 ^d | DABCO | EtOH | 5 | 72 |
| 16 ^e | DABCO | EtOH | 2 | 81 |

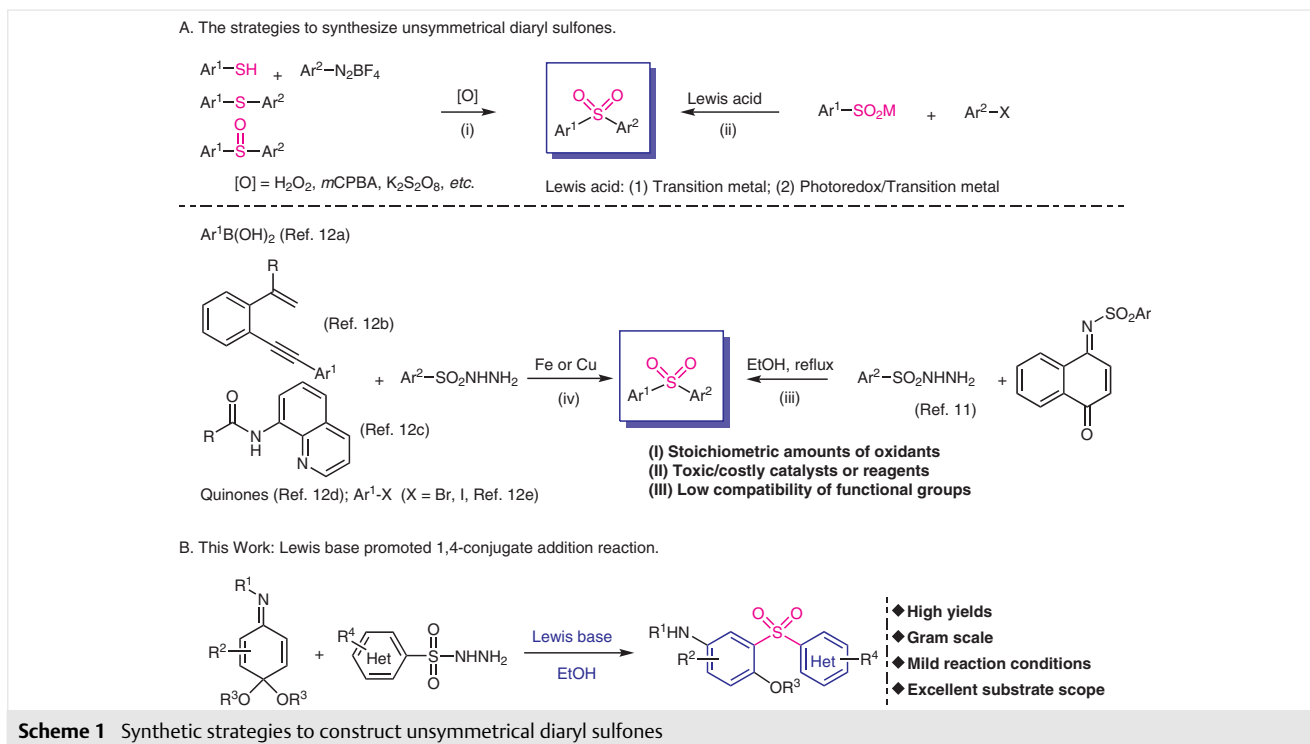
^a Reaction conditions: **1a** (0.1 mmol), **2a** (0.11 mmol), solvent (1.5 mL).

^b Catalyst (20 mol%).

^c Isolated yield based on **1a**.

^d Reaction temperature: 30 °C.

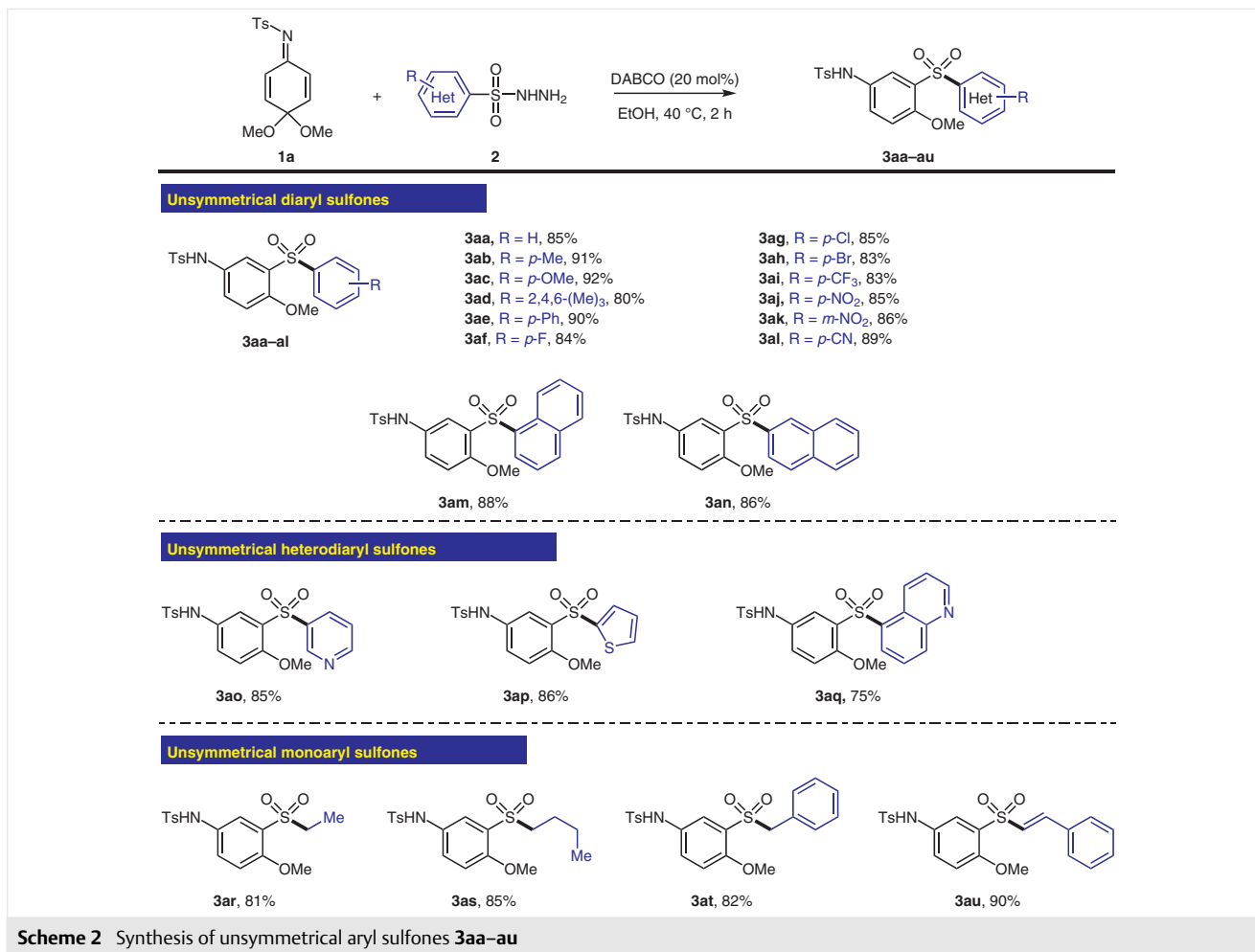
^e Reaction temperature: 50 °C.



quinone imines with tosyl hydrazine in refluxing ethanol to construct diaryl sulfones (Scheme 1, A, iii). Furthermore, in recent years, sulfonyl hydrazides, as stable, noncorrosive, readily accessible and odour-free precursors of the sulfone reagents, have been applied to construct unsymmetrical diaryl sulfones *via* Lewis acid (FeCl₂, Cu(OAc)₂, Cu(OTf)₂) catalysis (Scheme 1, A, iv).¹² Recently, quinones and quinone precursors as electrophiles were employed in reactions with sulfonyl hydrazides under mild conditions.¹³ Despite the various elegant strategies to obtain functionalized diaryl sulfones, there are still many deficiencies that need to be resolved, including the stoichiometric amounts of oxidants and toxic/costly/sensitive catalysts or reagents that are required in these reactive processes, the low functional-group compatibility and the low yields of some products in these transformations. In this context, considering the importance of unsymmetrical diaryl sulfones, an alternative strategy and technique with eco-friendliness and high efficiency for the preparation of unsymmetrical diaryl sulfones is still highly desirable. To our knowledge, Lewis base catalysis to construct unsymmetrical diaryl sulfones has not been reported up to now. In a continuation of our interest in constructing multifunctional molecules,¹⁴ we have accomplished the preparation of a series of unsymmetrical diaryl sulfones (diaryl and heterodiaryl sulfones), and even of unsymmetrical monoaryl sulfones (including aryl alkyl sulfones and aryl vinyl sulfones), *via* a Lewis base promoted, direct 1,4-conjugate addition/sulfonylation/alcohol elimination reaction sequence using quinone imine ketals with sulfonyl hydrazides in ethanol (Scheme 1, B).

Initially, our investigations focused on quinone imine ketal **1a** in combination with sulfonyl hydrazide **2a** as the model substrates to optimize the reaction conditions (Table 1). It was frustrating to observe that acid did not promote the reaction (Table 1, entries 1, 2). Subsequently, organic and inorganic base catalysts were screened; pleasingly, triethylamine and DABCO (triethylenediamine) provided the desired product **3aa** in 65% and 85% yield, respectively, with the latter showing a better catalytic performance (Table 1, entries 3–7). Then, a series of solvents (MeOH, toluene, CHCl₃, THF, MeCN, EtOAc, H₂O) was screened, which showed that the alcohols gave better results than other solvents (Table 1, entries 8–14). In addition, raising or lowering the reaction temperature did not give a better result (Table 1, entries 15, 16).

With the optimized reaction conditions in hand, the substrate scope of the reaction was investigated. Firstly, a wide variety of sulfonyl hydrazides **2** in which the substituents on the aromatic ring were electron-donating (Me, OMe, 2,4,6-(Me)₃, Ph) or electron-withdrawing (F, Cl, Br, NO₂, CN, CF₃) groups provided the corresponding products in excellent yields of 80–92% (Scheme 2, **3aa–al**). Notably, sterically hindered mesitylenesulfonyl hydrazide was well tolerated in the reaction, to provide the product **3ad** in 80% yield. In addition, α- and β-naphthalenesulfonyl hydrazide were also well compatible with the transformation, and delivered the desired products **3am** and **3an** in 88% and 86% yield, respectively. More importantly, 3-pyridinesulfonyl hydrazide, 2-thiophenesulfonyl hydrazide and 5-quinoline-sulfonyl hydrazide all survived as well in this transforma-

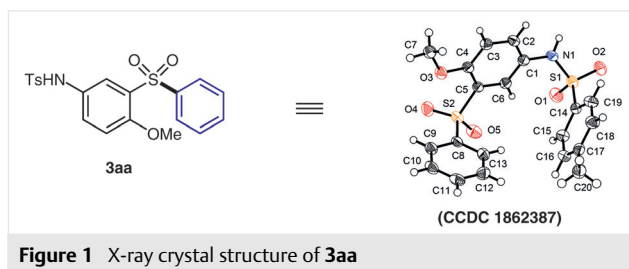


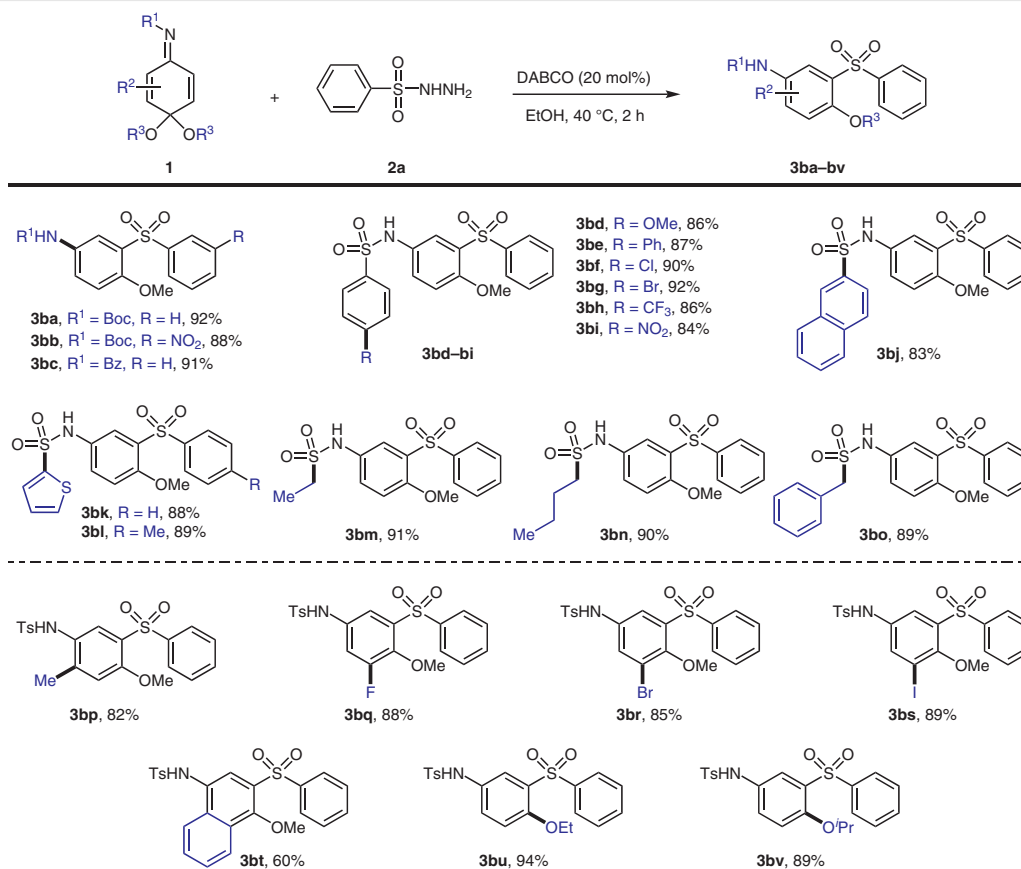
tion, delivering the unsymmetrical heterodiaryl sulfones **3ao–aq** in satisfactory yields. Furthermore, aliphatic sulfonyl hydrazides also proved to be suitable substrates under the standard reaction conditions, giving the corresponding aryl alkyl sulfones **3ar–at** in 81–85% yield (Scheme 2). To our delight, we obtained a most important aryl vinyl sulfone¹⁵ **3au** in 90% yield using styrenesulfonyl hydrazide as the sulfonylation reagent.

With the fruitful reaction conditions, we next turned our attention to broadening the substrate scope of the quinone imine ketals **1** in this transformation, as shown in Scheme 3. The protecting group R¹ could be altered from Ts to Boc or Bz, which resulted in 88–92% yield of **3ba–bc**. Furthermore, the protecting group R substituent at the *para*-position of the phenyl ring could be either electron rich or electron poor, which delivered the corresponding products **3bd–bi** in good to excellent yields of 84–92% (Scheme 3). Meanwhile, this protocol was also amenable to a wide scope of sulfonyl R¹ groups, such as β -naphthylsulfonyl, 2-thienylsulfonyl or alkylsulfonyl, which afforded the corre-

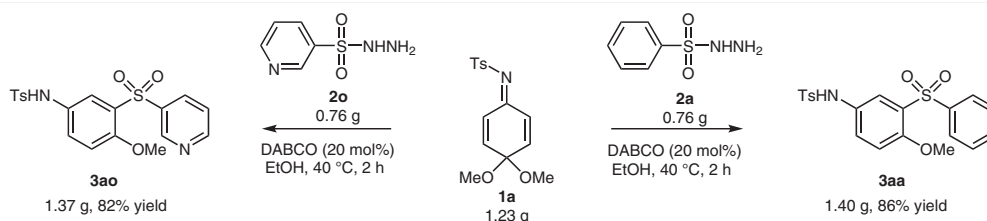
sponding unsymmetrical diaryl sulfones **3bj–bo** in generally acceptable yields. Subsequently, a series of quinone imine ketals with different R²/R³ groups was utilized for the reaction, with the R² variants providing the desired unsymmetrical diaryl sulfones **3bp–bt** in 60–89% yield. Furthermore, the alkoxy group OR³ could be elongated to OEt and OⁱPr, which gave the corresponding products in good yields (**3bu**, **3bv**; Scheme 3).

The relative configuration of **3aa** was determined by X-ray crystal analysis (Figure 1).¹⁶





Scheme 3 Synthesis of unsymmetrical diaryl sulfones **3ba-bv**



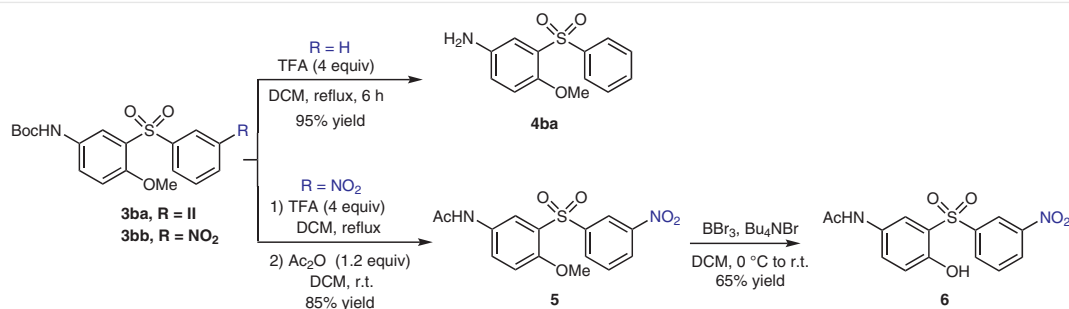
Scheme 4 Gram-scale reactions for the preparation of unsymmetrical diaryl and heterodaryl sulfones

To further demonstrate the potential utility of the reaction, benzenesulfonyl hydrazide (**2a**, 4.4 mmol) and 3-pyridinesulfonyl hydrazide (**2o**, 4.4 mmol) were selected as the aryl sulfone precursors to react with quinone imine ketal **1a** (4.0 mmol) (Scheme 4). To our delight, the yield of the corresponding unsymmetrical diaryl sulfone **3aa** and heterodaryl sulfone **3ao** remained reasonable. These results reveal that the protocol could be scaled up to a gram scale to provide a series of unsymmetrical diaryl and heterodaryl sulfones of potential significance.

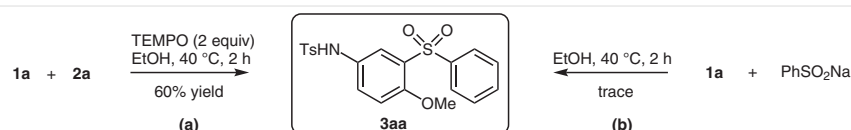
In addition, some synthetic transformations have been carried out. Firstly, deprotected compounds **4ba** and **4bb** were obtained in excellent yield under trifluoroacetic acid

conditions (Scheme 5). Also, the *N*-Boc group was converted into an *N*-acetyl group *via* a two-step reaction, which gave an 85% yield of the *N*-acetyl-substituted unsymmetrical diaryl sulfone **5**, which had not been investigated earlier (cf. Scheme 3). Subsequently, compound **5** underwent demethylation to provide a moderate 65% yield of compound **6**, which is the precursor compound of the 3,3'-sulfonyldianiline (Scheme 5).

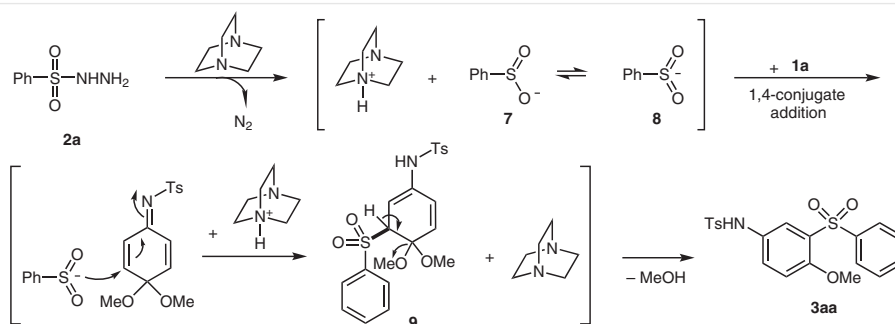
Furthermore, several experiments were conducted to investigate the mechanistic process. Firstly, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical scavenger was used in a radical-trapping experiment, and the result revealed that the transformation does not involve a free-



Scheme 5 Further synthetic applications



Scheme 6 Control experiments to investigate the mechanistic process

Scheme 7 Mechanistic hypothesis for the synthesis of unsymmetrical diaryl sulfone **3aa**

radical process (Scheme 6, a). When PhSO_2Na was used as the sulfonyl precursor for reaction with **1a**, only a trace of the product **3aa** can be detected (Scheme 6, b). Based on the aforementioned results and the report by Wang and co-workers¹⁷ that sulfonyl hydrazide could be quickly transformed into a sulfinyl anion, which is in resonance with the sulfur-centered anion, with N_2 release in the presence of imidazole, it is reasonable to speculate a possible reaction pathway, as depicted in Scheme 7. Firstly, sulfonyl hydrazide **2a** is quickly transformed into sulfinyl anion **7** which is in resonance with the sulfur-centered anion **8** in the presence of a Lewis base (DABCO), generating ammonium ions and releasing N_2 . Subsequently, the sulfur-centered anion **8** adds to quinone imine ketal **1a** via a 1,4-conjugate addition reaction to form intermediate **9**; then, the target product **3aa** is obtained by an alcohol elimination reaction (Scheme 7).

In summary, we have established an alternative approach with eco-friendliness and high efficiency for the synthesis of unsymmetrical diaryl and heterodiaryl sulfones, and even of aryl alkyl sulfones and aryl vinyl sul-

phones, in good to excellent yields. The reaction of sulfonyl hydrazides with quinone imine ketals catalyzed by DABCO in ethanol proceeds via a Lewis base promoted, direct 1,4-conjugate addition/sulfonylation/alcohol elimination reaction sequence. Further applications of these functionalized unsymmetrical diaryl and heterodiaryl sulfones are currently under investigation in our laboratory.

All received reagents and solvents were used without further purification unless otherwise stated. Melting points were determined on an XT-4A melting point apparatus and are uncorrected. NMR spectra were recorded on a Bruker 400 spectrometer (^1H : 400 MHz, ^{13}C : 100 MHz) with CDCl_3 as the solvent; chemical shifts (δ) are expressed in parts per million relative to the residual deuterated solvent signal, and coupling constants (J) are given in hertz. HRMS (ESI) analyses were performed on an Agilent LC/MSD TOF instrument.

Quinone Imine Ketals **1**; General Procedure¹⁸

To a stirred solution of the corresponding aniline (10 mmol, 1.0 equiv) in pyridine (20 mL) at 0 °C, the corresponding sulfonyl chloride (11 mmol, 1.1 equiv) was added slowly. The reaction mixture was allowed

to warm to ambient temperature, and was stirred overnight and monitored by TLC. When the aniline was completely consumed, the pyridine was evaporated under reduced pressure. The residue was quenched with EtOAc (10 mL) and 1 N HCl (10 mL), then the mixture was extracted with EtOAc (3 × 20 mL) and saturated NaHCO₃ (3 × 10 mL). The combined organic layers were washed with brine, dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc, 10:1–4:1) to give the corresponding *N*-protected aniline. To a solution of the *N*-protected aniline (2 mmol, 1.0 equiv) in distilled MeOH (20 mL) was added phenyliodine diacetate (PIDA) (2.4 mmol, 1.2 equiv) under nitrogen atmosphere, and the mixture was stirred at room temperature and monitored by TLC. When the *N*-protected aniline was completely consumed, the reaction was quenched with saturated NaHCO₃ (20 mL) and then the mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine (20 mL) and dried with anhydrous Na₂SO₄, then the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (petroleum ether/EtOAc, 15:1–6:1) to give the corresponding quinone imine ketal **1**.

Unsymmetrical Diaryl Sulfones **3**; General Procedure

A 10-mL round-bottom flask was charged with a quinone imine ketal **1** (0.1 mmol), a sulfonyl hydrazide **2** (0.11 mmol) and DABCO (0.02 mmol) in the presence of EtOH (2 mL) as solvent, and the solution was stirred for 1–2 h at 40 °C until the quinone imine ketal **1** was completely consumed, as indicated by TLC. The crude product was purified by flash column chromatography (petroleum ether/EtOAc, 10:1–2:1 as given in 43 cases, compds **3** below), which afforded the pure product **3** in 60–94% yield.

N-(4-Methoxy-3-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (**3aa**)

Yellow-white solid; yield: 35.5 mg (85%); mp 145–147 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.73 (s, 3 H, ArOCH₃), 6.71 (br, 1 H, NH), 6.84 (d, *J* = 8.0 Hz, 1 H, ArH), 7.24–7.26 (m, 2 H, ArH), 7.48–7.60 (m, 7 H, ArH), 7.84 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.2, 113.5, 124.7, 127.4, 128.4, 128.6, 129.1, 129.2, 129.8, 131.2, 133.3, 135.5, 140.8, 144.2, 155.1.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₀H₁₉NO₅S₂Na: 440.0597; found: 440.0596.

N-(4-Methoxy-3-tosylphenyl)-4-methylbenzenesulfonamide (**3ab**)

Yellow-white solid; yield: 39.2 mg (91%); mp 179–181 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.35 (s, 6 H, 2 ArCH₃), 3.66 (s, 3 H, ArOCH₃), 6.75 (d, *J* = 8.0 Hz, 1 H, ArH), 6.83 (br, 1 H, NH), 7.16–7.18 (m, 1 H, ArH), 7.19–7.20 (m, 1 H, ArH), 7.29 (d, *J* = 8.0 Hz, 1 H, ArH), 7.41–7.44 (m, 1 H, ArH), 7.51–7.53 (m, 3 H, ArH), 7.65 (d, *J* = 8.0 Hz, 2 H, ArH), 7.73 (d, *J* = 8.0 Hz, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 21.7, 56.2, 113.4, 124.6, 127.4, 128.3, 128.5, 129.2, 129.3, 129.8, 130.0, 130.9, 135.5, 137.9, 144.1, 144.2, 155.0.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₁H₂₁NO₅S₂Na: 454.0753; found: 454.0755.

N-(4-Methoxy-3-((4-methoxyphenyl)sulfonyl)phenyl)-4-methylbenzenesulfonamide (**3ac**)

Yellow-white solid; yield: 41.1 mg (92%); mp 163–165 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.75 (s, 3 H, ArOCH₃), 3.86 (s, 3 H, ArOCH₃), 6.83 (d, *J* = 12.0 Hz, 1 H, ArH), 6.88 (br, 1 H, NH), 6.93 (d, *J* = 8.0 Hz, 2 H, ArH), 7.24 (d, *J* = 8.0 Hz, 2 H, ArH), 7.47–7.50 (m, 1 H, ArH), 7.58–7.60 (m, 3 H, ArH), 7.78 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 55.7, 56.2, 113.4, 113.8, 124.4, 127.4, 129.2, 129.8, 130.7, 130.8, 132.2, 135.6, 144.2, 154.9, 163.4.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₁H₂₁NO₆S₂Na: 470.0702; found: 470.0701.

N-(3-(Mesitylsulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (**3ad**)

Yellow-white solid; yield: 36.7 mg (80%); mp 219–221 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.28 (s, 3 H, ArCH₃), 2.40 (s, 6 H, 2 ArCH₃), 2.41 (s, 3 H, ArCH₃), 3.63 (s, 3 H, ArOCH₃), 6.54 (br, 1 H, NH), 6.84 (d, *J* = 8.0 Hz, 1 H, ArH), 6.87 (m, 2 H, ArH), 7.24 (d, *J* = 8.0 Hz, 2 H, ArH), 7.51–7.60 (m, 4 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.0, 21.6, 22.3, 56.1, 113.5, 124.5, 127.3, 128.6, 129.9, 130.8, 131.1, 131.8, 134.2, 135.6, 140.1, 142.9, 144.2, 155.4.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₃H₂₅NO₅S₂Na: 482.1066; found: 482.1069.

N-(3-([1,1'-Biphenyl]-4-ylsulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (**3ae**)

Yellow-white solid; yield: 44.4 mg (90%); mp 94–96 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.76 (s, 3 H, ArOCH₃), 6.84 (br, 1 H, NH), 6.87 (d, *J* = 4.0 Hz, 1 H, ArH), 7.24 (m, 1 H, ArH), 7.40–7.53 (m, 5 H, ArH), 7.58–7.68 (m, 7 H, ArH), 7.90 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.2, 113.5, 124.6, 127.2, 127.3, 127.4, 128.6, 129.0, 129.1, 129.4, 129.8, 131.1, 135.6, 139.2, 139.3, 144.2, 146.2, 155.1.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₆H₂₃NO₅S₂Na: 516.0910; found: 516.0912.

N-(3-((4-Fluorophenyl)sulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (**3af**)

Yellow-white solid; yield: 36.5 mg (84%); mp 145–147 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.75 (s, 3 H, ArOCH₃), 6.79 (br, 1 H, NH), 6.85 (d, *J* = 12.0 Hz, 1 H, ArH), 7.15 (t, *J* = 8.0 Hz, 2 H, ArH), 7.24–7.27 (m, 2 H, ArH), 7.50–7.52 (m, 1 H, ArH), 7.59–7.61 (m, 3 H, ArH), 7.85–7.88 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.2, 113.5, 115.8, 116.0, 124.5, 127.4, 129.0, 129.4, 129.8, 131.1, 131.3, 131.4, 135.6, 136.8, 144.3, 154.9, 164.3.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₀H₁₈FNO₅S₂Na: 458.0503; found: 458.0505.

N-(3-((4-Chlorophenyl)sulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (**3ag**)

Yellow-white solid; yield: 38.3 mg (85%); mp 171–173 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.44 (s, 3 H, ArCH₃), 3.77 (s, 3 H, ArOCH₃), 6.85–6.97 (m, 2 H, ArH), 7.26 (m, 2 H, ArH), 7.46–7.63 (m, 6 H, ArH), 7.80 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.3, 113.5, 124.5, 127.4, 128.7, 128.9, 129.5, 129.9, 130.0, 131.2, 135.5, 139.2, 140.0, 144.3, 154.9.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈ClNO₅S₂Na: 474.0207; found: 474.0207.

***N*-(3-((4-Bromophenyl)sulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (3ah)**

Yellow-white solid; yield: 41.0 mg (83%); mp 163–165 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.41 (s, 3 H, ArCH₃), 3.75 (s, 3 H, ArOCH₃), 6.84 (d, J = 12.0 Hz, 1 H, ArH), 7.09 (br, 1 H, NH), 7.23–7.27 (m, 2 H, ArH), 7.49–7.51 (m, 1 H, ArH), 7.60–7.63 (m, 5 H, ArH), 7.70–7.72 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.2, 113.5, 124.4, 127.4, 128.5, 128.6, 129.5, 129.7, 129.8, 130.0, 131.1, 131.9, 132.6, 135.5, 139.8, 144.3, 154.9.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈BrNO₅S₂Na: 517.9702; found: 517.9705.

***N*-(4-Methoxy-3-((4-(trifluoromethyl)phenyl)sulfonyl)phenyl)-4-methylbenzenesulfonamide (3ai)**

Yellow-white solid; yield: 40.3 mg (83%); mp 160–162 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.43 (s, 3 H, ArCH₃), 3.75 (s, 3 H, ArOCH₃), 6.86 (d, J = 12.0 Hz, 1 H, ArH), 6.89 (br, 1 H, NH), 7.27 (m, 2 H, ArH), 7.51–7.53 (m, 1 H, ArH), 7.61–7.63 (m, 3 H, ArH), 7.73–7.75 (m, 2 H, ArH), 7.97–7.99 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.3, 113.5, 124.6, 125.6, 125.7, 125.8, 127.4, 128.2, 129.0, 129.6, 129.9, 131.4, 134.7, 135.0, 135.5, 144.3, 144.4, 155.0.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₁H₁₈F₃NO₅S₂Na: 508.0471; found: 508.0475.

***N*-(4-Methoxy-3-((4-nitrophenyl)sulfonyl)phenyl)-4-methylbenzenesulfonamide (3aj)**

Yellow-white solid; yield: 39.3 mg (85%); mp 135–137 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.43 (s, 3 H, ArCH₃), 3.75 (s, 3 H, ArOCH₃), 6.86 (d, J = 12.0 Hz, 1 H, ArH), 7.17 (br, 1 H, NH), 7.26–7.28 (m, 2 H, ArH), 7.50–7.53 (m, 1 H, ArH), 7.63–7.65 (m, 2 H, ArH), 7.71–7.72 (m, 1 H, ArH), 8.03–8.06 (m, 2 H, ArH), 8.30–8.32 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.3, 113.6, 123.8, 124.5, 127.4, 127.7, 129.8, 129.9, 131.4, 135.5, 144.4, 146.5, 150.4, 154.9.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈N₂O₇S₂Na: 485.0448; found: 485.0450.

***N*-(4-Methoxy-3-((3-nitrophenyl)sulfonyl)phenyl)-4-methylbenzenesulfonamide (3ak)**

Yellow-white solid; yield: 39.7 mg (86%); mp 227–229 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.44 (s, 3 H, ArCH₃), 3.79 (s, 3 H, ArOCH₃), 6.59 (br, 1 H, NH), 6.88 (d, J = 8.0 Hz, 1 H, ArH), 7.30 (d, J = 8.0 Hz, 2 H, ArH), 7.55–7.58 (m, 1 H, ArH), 7.60–7.62 (m, 3 H, ArH), 7.72 (t, J = 8.0 Hz, 1 H, ArH), 8.23 (d, J = 8.0 Hz, 1 H, ArH), 8.44–8.46 (m, 1 H, ArH), 8.73 (m, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.3, 113.6, 124.0, 124.6, 127.3, 127.8, 127.9, 129.5, 129.9, 130.0, 132.0, 134.2, 135.4, 142.8, 144.6, 148.0, 155.0.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈N₂O₇S₂Na: 485.0448; found: 485.0450.

***N*-(3-((4-Cyanophenyl)sulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (3al)**

Yellow-white solid; yield: 39.3 mg (89%); mp 147–149 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.74 (s, 3 H, ArOCH₃), 6.85 (d, J = 8.0 Hz, 1 H, ArH), 7.10 (br, 1 H, NH), 7.25–7.28 (m, 2 H, ArH), 7.49–7.52 (m, 1 H, ArH), 7.64 (d, J = 8.0 Hz, 2 H, ArH), 7.68–7.69 (m, 1 H, ArH), 7.77–7.79 (m, 2 H, ArH), 7.96–7.99 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.3, 113.6, 116.9, 117.3, 124.5, 127.4, 127.8, 129.1, 129.7, 129.9, 131.3, 132.4, 135.5, 144.4, 145.0, 154.9.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₁H₁₈N₂O₅S₂Na: 465.0549; found: 465.0550.

***N*-(4-Methoxy-3-(naphthalen-1-ylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3am)**

Yellow-white solid; yield: 41.1 mg (88%); mp 238–240 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.54 (s, 3 H, ArOCH₃), 6.67 (br, 1 H, NH), 6.74 (d, J = 12.0 Hz, 1 H, ArH), 7.23–7.25 (m, 2 H, ArH), 7.39–7.47 (m, 2 H, ArH), 7.50–7.53 (m, 1 H, ArH), 7.60–7.64 (m, 3 H, ArH), 7.89–7.94 (m, 2 H, ArH), 8.10 (d, J = 8.0 Hz, 1 H, ArH), 8.31 (d, J = 8.0 Hz, 1 H, ArH), 8.50 (d, J = 8.0 Hz, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.0, 113.5, 123.9, 124.0, 124.8, 126.5, 127.3, 128.2, 128.4, 129.0, 129.2, 129.7, 129.9, 130.7, 131.5, 133.9, 135.0, 135.3, 135.7, 144.2, 155.3.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₄H₂₁NO₅S₂Na: 490.0753; found: 490.0752.

***N*-(4-Methoxy-3-(naphthalen-2-ylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3an)**

Yellow-white solid; yield: 40.1 mg (86%); mp 139–141 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.43 (s, 3 H, ArCH₃), 3.70 (s, 3 H, ArOCH₃), 6.80–6.87 (m, 2 H, ArH), 7.24–7.26 (m, 2 H, ArH), 7.49–7.52 (m, 1 H, ArH), 7.60–7.74 (m, 6 H, ArH), 7.88–7.90 (m, 2 H, ArH), 7.96–7.98 (m, 1 H, ArH), 8.52 (m, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.2, 113.4, 123.3, 124.7, 127.4, 127.5, 127.9, 128.7, 129.2, 129.3, 129.4, 129.8, 130.3, 131.1, 132.0, 135.1, 135.6, 137.6, 144.2, 155.1.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₄H₂₁NO₅S₂Na: 490.0753; found: 490.0752.

***N*-(4-Methoxy-3-(pyridin-3-ylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3ao)**

Yellow-white solid; yield: 35.5 mg (85%); mp 174–176 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.77 (s, 3 H, ArOCH₃), 6.86 (d, J = 12.0 Hz, 1 H, ArH), 7.24–7.27 (m, 2 H, ArH), 7.45–7.50 (m, 2 H, ArH), 7.53–7.56 (m, 1 H, ArH), 7.61 (d, J = 8.0 Hz, 2 H, ArH), 7.65–7.66 (m, 1 H, ArH), 8.21 (d, J = 8.0 Hz, 1 H, ArH), 8.83–8.84 (m, 1 H, ArH), 9.02 (m, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.3, 113.5, 123.5, 124.4, 127.3, 128.3, 129.8, 129.9, 131.5, 135.5, 136.6, 137.5, 144.4, 149.3, 153.4, 154.8.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₁₉H₁₈N₂O₅S₂Na: 441.0549; found: 441.0547.

***N*-(4-Methoxy-3-(thiophen-2-ylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3ap)**

Yellow-white solid; yield: 36.4 mg (86%); mp 179–181 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.41 (s, 3 H, ArCH₃), 3.88 (s, 3 H, ArOCH₃), 6.57 (br, 1 H, NH), 6.90 (d, *J* = 8.0 Hz, 1 H, ArH), 7.07–7.09 (m, 1 H, ArH), 7.23–7.25 (m, 2 H, ArH), 7.52–7.59 (m, 4 H, ArH), 7.64–7.66 (m, 1 H, ArH), 7.68–7.70 (m, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.2, 113.4, 124.4, 127.2, 127.3, 129.2, 129.6, 129.9, 131.2, 133.9, 134.4, 135.5, 141.9, 144.3, 155.2.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₈H₁₇NO₅S₃Na: 446.0161; found: 446.0160.

***N*-(4-Methoxy-3-(quinolin-5-ylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3aq)**

Yellow-white solid; yield: 35.1 mg (75%); mp 192–194 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.54 (s, 3 H, ArOCH₃), 6.72–6.77 (m, 2 H, ArH), 7.25 (m, 1 H, ArH), 7.40 (m, 1 H, ArH), 7.52–7.72 (m, 5 H, ArH), 7.97 (m, 1 H, ArH), 8.08–8.10 (m, 1 H, ArH), 8.19 (m, 1 H, ArH), 8.69–8.71 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.2, 113.0, 121.9, 125.4, 126.3, 127.3, 128.7, 129.1, 129.9, 130.2, 133.0, 134.3, 136.0, 136.5, 136.6, 137.0, 144.1, 151.1, 154.9.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₃H₂₀N₂O₅S₂Na: 491.0706; found: 491.0709.

***N*-(3-(Ethylsulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (3ar)**

Yellow-white solid; yield: 29.9 mg (81%); mp 136–138 °C.

¹H NMR (400 MHz, CDCl₃): δ = 1.13 (t, *J* = 8.0 Hz, 3 H, CH₂CH₃), 2.37 (s, 3 H, ArCH₃), 3.31 (q, *J* = 8.0, 16.0 Hz, 2 H, CH₂CH₃), 3.94 (s, 3 H, ArOCH₃), 6.92 (br, 1 H, NH), 6.98 (d, *J* = 8.0 Hz, 1 H, ArH), 7.22 (d, *J* = 8.0 Hz, 2 H, ArH), 7.40 (m, 1 H, ArH), 7.58–7.62 (m, 3 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 7.2, 21.6, 48.6, 56.6, 113.3, 125.3, 126.2, 127.3, 129.7, 129.8, 130.6, 135.5, 144.2, 155.2.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₆H₁₉NO₅S₂Na: 392.0597; found: 392.0599.

***N*-(3-(Butylsulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (3as)**

Yellow-white solid; yield: 33.7 mg (85%); mp 120–122 °C.

¹H NMR (400 MHz, CDCl₃): δ = 0.88 (t, *J* = 8.0 Hz, 3 H, CH₂CH₃), 1.32–1.41 (m, 2 H, CH₂), 1.49–1.57 (m, 2 H, CH₂), 2.37 (s, 3 H, ArCH₃), 3.28–3.32 (m, 2 H, SO₂CH₂), 3.94 (s, 3 H, ArOCH₃), 6.98 (d, *J* = 8.0 Hz, 1 H, ArH), 7.07 (br, 1 H, NH), 7.22 (d, *J* = 8.0 Hz, 2 H, ArH), 7.42–7.43 (m, 1 H, ArH), 7.59–7.61 (m, 3 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 13.5, 21.5, 21.6, 24.4, 54.0, 56.7, 113.3, 124.9, 127.0, 127.3, 129.7, 129.8, 130.4, 135.6, 144.2, 155.1.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₈H₂₃NO₅S₂Na: 420.0910; found: 420.0911.

***N*-(3-(Benzylsulfonyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (3at)**

Yellow-white solid; yield: 35.3 mg (82%); mp 212–214 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.39 (s, 3 H, ArCH₃), 4.03 (s, 3 H, ArOCH₃), 4.54 (s, 2 H, CH₂), 6.36 (br, 1 H, NH), 6.99 (d, *J* = 8.0 Hz, 1 H, ArH), 7.09–7.27 (m, 8 H, ArH), 7.45–7.47 (m, 2 H, ArH), 7.54–7.56 (m, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.8, 60.5, 113.2, 125.5, 126.3, 127.1, 127.9, 128.6, 128.8, 129.5, 129.8, 130.6, 130.9, 135.5, 144.2, 155.3.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₁H₂₁NO₅S₂Na: 454.0753; found: 454.0754.

***N*-(4-Methoxy-3-((*E*)-styrylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3au)**

Yellow-white solid; yield: 39.9 mg (90%); mp 208–210 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.38 (s, 3 H, ArCH₃), 3.93 (s, 3 H, ArOCH₃), 6.70 (br, 1 H, NH), 6.94 (d, *J* = 8.0 Hz, 1 H, CH=CH), 7.04 (d, *J* = 16.0 Hz, 1 H, CH=CH), 7.23 (d, *J* = 8.0 Hz, 2 H, ArH), 7.40–7.45 (m, 3 H, ArH), 7.48–7.59 (m, 4 H, ArH), 7.61–7.65 (m, 3 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.6, 56.6, 113.4, 123.9, 126.2, 127.3, 128.6, 129.0, 129.1, 129.6, 129.8, 130.4, 131.3, 132.6, 135.6, 144.1, 144.3, 155.2.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₂H₂₁NO₅S₂Na: 466.0753; found: 466.0757.

***tert*-Butyl (4-Methoxy-3-(phenylsulfonyl)phenyl)carbamate (3ba)**

Yellow-white solid; yield: 33.4 mg (92%); mp 166–168 °C.

¹H NMR (400 MHz, CDCl₃): δ = 1.51 (s, 9 H, 3 CH₃), 3.71 (s, 3 H, ArOCH₃), 6.67 (br, 1 H, NH), 6.85 (d, *J* = 8.0 Hz, 1 H, ArH), 7.46–7.50 (m, 2 H, ArH), 7.57 (d, *J* = 8.0 Hz, 1 H, ArH), 7.82 (m, 1 H, ArH), 7.95–7.97 (m, 3 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 28.3, 56.3, 81.0, 113.4, 126.3, 128.4, 128.5, 129.0, 131.7, 133.1, 141.2, 152.8, 153.0.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₈H₂₁NO₅SNa: 386.1033; found: 386.1035.

***tert*-Butyl (4-Methoxy-3-((3-nitrophenyl)sulfonyl)phenyl)carbamate (3bb)**

Yellow-white solid; yield: 35.9 mg (88%); mp 195–197 °C.

¹H NMR (400 MHz, CDCl₃): δ = 1.53 (s, 9 H, 3 CH₃), 3.78 (s, 3 H, ArOCH₃), 6.67 (br, 1 H, NH), 6.88 (d, *J* = 8.0 Hz, 1 H, ArH), 7.71 (t, *J* = 8.0 Hz, 1 H, ArH), 7.80 (m, 1 H, ArH), 8.01 (m, 1 H, ArH), 8.30 (d, *J* = 8.0 Hz, 1 H, ArH), 8.42–8.45 (m, 1 H, ArH), 8.86–8.87 (m, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 28.3, 56.3, 81.2, 113.3, 120.4, 124.1, 127.0, 127.5, 127.6, 129.9, 132.0, 134.1, 143.3, 147.9, 152.7, 152.9.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₈H₂₀N₂O₇SNa: 431.0883; found: 431.0885.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)benzamide (3bc)**

Yellow-white solid; yield: 33.4 mg (91%); mp 176–178 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.74 (s, 3 H, ArOCH₃), 6.93 (d, *J* = 8.0 Hz, 1 H, ArH), 7.38 (t, *J* = 8.0 Hz, 2 H, ArH), 7.45–7.50 (m, 3 H, ArH), 7.56–7.59 (m, 1 H, ArH), 7.88 (d, *J* = 8.0 Hz, 2 H, ArH), 7.95 (d, *J* = 8.0 Hz, 2 H, ArH), 8.21 (m, 1 H, ArH), 8.34–8.37 (m, 1 H, ArH), 8.58 (br, 1 H, NH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.3, 121.7, 127.2, 128.3, 128.4, 128.6, 128.7, 131.6, 131.9, 133.2, 140.9, 153.6, 166.1.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₀H₁₇NO₄SNa: 390.0770; found: 390.0771.

4-Methoxy-*N*-(4-methoxy-3-(phenylsulfonyl)phenyl)benzenesulfonamide (3bd)

Yellow-white solid; yield: 37.2 mg (86%); mp 106–108 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.73 (s, 3 H, ArOCH₃), 3.87 (s, 3 H, ArOCH₃), 6.72 (br, 1 H, NH), 6.84 (d, *J* = 8.0 Hz, 1 H, ArH), 6.90–6.92 (m, 2 H, ArH), 7.46–7.53 (m, 3 H, ArH), 7.57–7.65 (m, 4 H, ArH), 7.83 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 55.7, 56.2, 113.5, 114.4, 124.8, 128.4, 128.6, 129.2, 129.4, 129.6, 130.0, 131.2, 133.3, 140.8, 155.1, 163.4.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₀H₁₉NO₆S₂Na: 456.0546; found: 456.0547.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)-[1,1'-biphenyl]-4-sulfonamide (3be)**

Yellow-white solid; yield: 41.7 mg (87%); mp 182–184 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.73 (s, 3 H, ArOCH₃), 6.84 (d, *J* = 8.0 Hz, 1 H, ArH), 7.09 (br, 1 H, NH), 7.32 (d, *J* = 8.0 Hz, 2 H, ArH), 7.42–7.67 (m, 10 H, ArH), 7.78 (d, *J* = 8.0 Hz, 4 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.5, 124.9, 127.4, 127.8, 127.9, 128.4, 128.6, 128.7, 129.1, 129.2, 131.3, 133.3, 136.9, 139.1, 140.6, 146.1, 155.2.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₅H₂₁NO₅S₂Na: 502.0753; found: 502.0755.

4-Chloro-*N*-(4-methoxy-3-(phenylsulfonyl)phenyl)benzenesulfonamide (3bf)

Yellow-white solid; yield: 39.3 mg (90%); mp 151–153 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.75 (s, 3 H, ArOCH₃), 6.85–6.87 (m, 2 H, ArH), 7.42 (d, *J* = 8.0 Hz, 2 H, ArH), 7.49–7.53 (m, 3 H, ArH), 7.58–7.64 (m, 4 H, ArH), 7.83 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.5, 125.1, 128.5, 128.6, 128.7, 128.8, 129.5, 131.5, 133.4, 137.0, 139.8, 140.6, 155.4.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₉H₁₆ClNO₅S₂Na: 460.0051; found: 460.0054.

4-Bromo-*N*-(4-methoxy-3-(phenylsulfonyl)phenyl)benzenesulfonamide (3bg)

Yellow-white solid; yield: 44.2 mg (92%); mp 183–185 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.76 (s, 3 H, ArOCH₃), 6.79 (br, 1 H, NH), 6.87 (d, *J* = 12.0 Hz, 1 H, ArH), 7.50–7.55 (m, 5 H, ArH), 7.58–7.63 (m, 4 H, ArH), 7.83 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.5, 125.1, 128.4, 128.5, 128.6, 128.7, 128.9, 129.3, 131.6, 132.5, 133.4, 137.5, 140.5, 155.4.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₉H₁₆BrNO₅S₂Na: 503.9545; found: 503.9544.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)-4-(trifluoromethyl)benzenesulfonamide (3bh)**

Yellow-white solid; yield: 40.5 mg (86%); mp 171–173 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.73 (s, 3 H, ArOCH₃), 6.85 (d, *J* = 8.0 Hz, 1 H, ArH), 7.46–7.53 (m, 4 H, ArH), 7.58–7.61 (m, 1 H, ArH), 7.67–7.71 (m, 3 H, ArH), 7.81–7.86 (m, 4 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.6, 121.8, 124.5, 124.8, 126.3 (q, *J* = 12.0 Hz), 128.0, 128.4, 128.7, 128.8, 129.1, 131.2, 133.5, 134.5 (q, *J* = 12.0 Hz), 140.4, 142.1, 155.3.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₀H₁₆F₃NO₅S₂Na: 494.0314; found: 494.0315.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)-4-nitrobenzenesulfonamide (3bi)**

Yellow-white solid; yield: 37.6 mg (84%); mp 89–91 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.76 (s, 3 H, ArOCH₃), 6.87 (d, *J* = 8.0 Hz, 1 H, ArH), 7.49–7.62 (m, 5 H, ArH), 7.69 (m, 1 H, ArH), 7.83 (d, *J* = 8.0 Hz, 2 H, ArH), 7.89 (d, *J* = 8.0 Hz, 2 H, ArH), 8.25 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.3, 113.7, 124.3, 124.9, 128.2, 128.4, 128.7, 128.8, 129.4, 131.3, 133.6, 140.3, 144.3, 150.2, 155.4.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₉H₁₆N₂O₇S₂Na: 471.0291; found: 471.0290.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)naphthalene-2-sulfonamide (3bj)**

Yellow-white solid; yield: 37.6 mg (83%); mp 170–172 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.69 (s, 3 H, ArOCH₃), 6.80 (d, *J* = 12.0 Hz, 1 H, ArH), 7.21 (br, 1 H, NH), 7.32–7.35 (m, 2 H, ArH), 7.50–7.51 (m, 2 H, ArH), 7.59 (t, *J* = 8.0 Hz, 1 H, ArH), 7.63–7.67 (m, 4 H, ArH), 7.73–7.75 (m, 1 H, ArH), 7.86–7.91 (m, 3 H, ArH), 8.30 (s, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.5, 122.3, 124.9, 127.7, 128.0, 128.3, 128.6, 129.0, 129.1, 129.4, 129.7, 131.3, 132.0, 133.2, 135.0, 135.3, 140.5, 155.1.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₂₃H₁₉NO₅S₂Na: 476.0597; found: 476.0596.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)thiophene-2-sulfonamide (3bk)**

Yellow-white solid; yield: 36.0 mg (88%); mp 127–129 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.76 (s, 3 H, ArOCH₃), 6.75 (br, 1 H, NH), 6.88 (d, *J* = 8.0 Hz, 1 H, ArH), 6.88 (t, *J* = 4.0 Hz, 1 H, ArH), 7.46–7.51 (m, 3 H, ArH), 7.55–7.61 (m, 3 H, ArH), 7.67–7.68 (m, 1 H, ArH), 7.88 (d, *J* = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.2, 113.5, 125.1, 127.6, 128.5, 128.6, 128.7, 129.3, 131.7, 132.9, 133.2, 133.3, 138.8, 140.7, 155.5.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₇H₁₅NO₅S₂Na: 432.0005; found: 432.0001.

***N*-(4-Methoxy-3-tosylphenyl)thiophene-2-sulfonamide (3bl)**

Yellow-white solid; yield: 37.6 mg (89%); mp 143–144 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.77 (s, 3 H, ArOCH₃), 6.64 (br, 1 H, NH), 6.88 (d, *J* = 12.0 Hz, 1 H, ArH), 7.05–7.07 (m, 1 H, ArH), 7.27–7.29 (m, 2 H, ArH), 7.44–7.46 (m, 1 H, ArH), 7.54–7.57 (m, 1 H, ArH), 7.60–7.63 (m, 2 H, ArH), 7.74–7.76 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 56.2, 113.4, 125.0, 127.6, 128.5, 128.6, 129.3, 129.6, 131.6, 132.9, 133.2, 137.7, 138.8, 144.3, 155.5.

HRMS (ESI-TOF): *m/z* [M + Na]⁺ calcd for C₁₈H₁₇NO₅S₂Na: 446.0161; found: 446.0160.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)ethanesulfonamide (3bm)**

Yellow-white solid; yield: 32.3 mg (91%); mp 181–183 °C.

¹H NMR (400 MHz, CDCl₃): δ = 1.41 (t, *J* = 8.0 Hz, 3 H, CH₂CH₃), 3.13 (q, *J* = 8.0 Hz, 2 H, CH₂CH₃), 3.75 (s, 3 H, ArOCH₃), 6.77 (br, 1 H, NH), 6.91 (d, *J* = 12.0 Hz, 1 H, ArH), 7.51 (t, *J* = 8.0 Hz, 2 H, ArH), 7.58–7.62 (m, 2 H, ArH), 7.96–7.97 (m, 3 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 8.3, 46.4, 56.3, 113.8, 123.7, 128.5, 128.7, 129.5, 129.6, 130.2, 133.4, 140.6, 154.9.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₁₅H₁₇NO₅S₂Na: 378.0440; found: 378.0441.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)butane-1-sulfonamide (3bn)**

Yellow-white solid; yield: 34.5 mg (90%); mp 107–109 °C.

¹H NMR (400 MHz, CDCl₃): δ = 0.92 (t, J = 8.0 Hz, 3 H, CH₂CH₃), 1.40–1.48 (m, 2 H, CH₂), 1.78–1.86 (m, 2 H, CH₂), 3.06–3.12 (m, 2 H, CH₂), 3.75 (s, 3 H, ArOCH₃), 6.90 (d, J = 8.0 Hz, 1 H, ArH), 7.15 (br, 1 H, NH), 7.48–7.53 (m, 2 H, ArH), 7.58–7.61 (m, 2 H, ArH), 7.95–7.99 (m, 3 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 13.6, 21.5, 25.4, 51.6, 56.3, 113.8, 123.6, 128.5, 128.7, 129.4, 129.8, 130.0, 133.4, 140.7, 154.8.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₁₇H₂₁NO₅S₂Na: 406.0753; found: 406.0750.

***N*-(4-Methoxy-3-(phenylsulfonyl)phenyl)-1-phenylmethanesulfonamide (3bo)**

Yellow-white solid; yield: 37.1 mg (89%); mp 128–130 °C.

¹H NMR (400 MHz, CDCl₃): δ = 3.75 (s, 3 H, ArOCH₃), 4.34 (s, 2 H, CH₂), 6.79 (br, 1 H, NH), 6.85 (d, J = 8.0 Hz, 1 H, ArH), 7.33–7.38 (m, 5 H, ArH), 7.44–7.47 (m, 1 H, ArH), 7.51 (t, J = 8.0 Hz, 2 H, ArH), 7.60 (t, J = 8.0 Hz, 1 H, ArH), 7.84 (m, 1 H, ArH), 7.96–7.97 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 56.3, 58.2, 113.7, 123.3, 128.3, 128.5, 128.7, 129.0, 129.1, 129.4, 129.5, 129.7, 130.9, 133.4, 140.7, 154.6.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₉NO₅S₂Na: 440.0597; found: 440.0594.

***N*-(4-Methoxy-2-methyl-5-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3bp)**

Yellow-white solid; yield: 35.3 mg (82%); mp 118–120 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.29 (s, 3 H, ArCH₃), 2.46 (s, 3 H, ArCH₃), 3.74 (s, 3 H, ArOCH₃), 6.28 (br, 1 H, NH), 6.70 (s, 1 H, ArH), 7.31 (d, J = 8.0 Hz, 2 H, ArH), 7.46–7.49 (m, 2 H, ArH), 7.51 (s, 1 H, ArH), 7.56–7.59 (m, 1 H, ArH), 7.63 (d, J = 8.0 Hz, 2 H, ArH), 7.81–7.83 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 19.0, 21.7, 56.1, 114.8, 126.8, 126.9, 127.6, 128.3, 128.5, 128.6, 129.9, 133.1, 136.0, 141.2, 144.3, 144.9, 155.7.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₁H₂₁NO₅S₂Na: 454.0753; found: 454.0755.

***N*-(3-Fluoro-4-methoxy-5-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3bq)**

Yellow-white solid; yield: 38.3 mg (88%); mp 176–178 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.43 (s, 3 H, ArCH₃), 3.94 (s, 3 H, ArOCH₃), 7.20 (br, 1 H, NH), 7.29 (d, J = 8.0 Hz, 2 H, ArH), 7.49 (t, J = 8.0 Hz, 2 H, ArH), 7.59–7.62 (m, 1 H, ArH), 7.66 (m, 1 H, ArH), 7.69–7.71 (m, 3 H, ArH), 7.85 (d, J = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 62.6, 119.6, 121.3, 127.4, 128.2, 129.0, 130.1, 131.6, 133.7, 133.8, 135.4, 136.9, 140.5, 144.7, 152.2.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈FNO₅S₂Na: 458.0503; found: 458.0500.

***N*-(3-Bromo-4-methoxy-5-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3br)**

Yellow-white solid; yield: 42.0 mg (85%); mp 160–162 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.43 (s, 3 H, ArCH₃), 3.93 (s, 3 H, ArOCH₃), 7.28–7.32 (m, 3 H, ArH), 7.49 (t, J = 8.0 Hz, 2 H, ArH), 7.59–7.62 (m, 1 H, ArH), 7.67 (m, 1 H, ArH), 7.70–7.72 (m, 3 H, ArH), 7.84–7.86 (m, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 62.6, 119.6, 121.2, 127.4, 128.2, 129.0, 130.0, 131.6, 133.8, 135.4, 136.9, 140.4, 144.7, 152.2.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈BrNO₅S₂Na: 517.9702; found: 517.9705.

***N*-(3-Iodo-4-methoxy-5-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3bs)**

Yellow-white solid; yield: 48.2 mg (89%); mp 181–183 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.42 (s, 3 H, ArCH₃), 3.94 (s, 3 H, ArOCH₃), 7.27–7.29 (m, 2 H, ArH), 7.47–7.50 (m, 3 H, ArH), 7.59 (t, J = 8.0 Hz, 1 H, ArH), 7.71 (d, J = 8.0 Hz, 2 H, ArH), 7.75 (d, J = 4.0 Hz, 1 H, ArH), 7.83–7.85 (m, 2 H, ArH), 7.89 (d, J = 4.0 Hz, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.7, 63.2, 93.8, 122.3, 127.4, 128.2, 129.0, 130.0, 133.7, 134.3, 135.4, 136.0, 140.4, 144.6, 154.8.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₀H₁₈INO₅S₂Na: 565.9563; found: 565.9565.

***N*-(4-Methoxy-3-(phenylsulfonyl)naphthalen-1-yl)-4-methylbenzenesulfonamide (3bt)**

Yellow-white solid; yield: 28.0 mg (60%); mp 185–187 °C.

¹H NMR (400 MHz, CDCl₃): δ = 2.46 (s, 3 H, ArCH₃), 4.12 (s, 3 H, ArOCH₃), 6.62 (br, 1 H, NH), 7.31 (d, J = 8.0 Hz, 2 H, ArH), 7.48 (t, J = 8.0 Hz, 2 H, ArH), 7.56–7.61 (m, 3 H, ArH), 7.66–7.68 (m, 3 H, ArH), 7.88 (d, J = 8.0 Hz, 2 H, ArH), 8.07 (d, J = 12.0 Hz, 1 H, ArH), 8.24 (d, J = 8.0 Hz, 1 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.8, 65.1, 122.1, 123.8, 124.2, 127.8, 127.9, 128.1, 128.9, 129.2, 129.9, 130.0, 133.5, 141.8, 144.6, 155.8.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₄H₂₁NO₅S₂Na: 490.0753; found: 490.0756.

***N*-(4-Ethoxy-3-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3bu)**

Yellow-white solid; yield: 40.5 mg (94%); mp 154–156 °C.

¹H NMR (400 MHz, CDCl₃): δ = 1.28 (t, J = 12.0 Hz, 3 H, CH₂CH₃), 3.69 (s, 3 H, ArCH₃), 3.93 (q, J = 12.0 Hz, 2 H, CH₂CH₃), 6.80 (d, J = 12.0 Hz, 1 H, ArH), 6.90 (br, 1 H, NH), 7.24–7.27 (m, 2 H, ArH), 7.45–7.51 (m, 3 H, ArH), 7.57–7.63 (m, 4 H, ArH), 7.84 (d, J = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 14.3, 21.7, 65.0, 113.9, 124.7, 127.4, 128.5, 128.6, 128.8, 129.0, 129.8, 131.2, 133.2, 135.5, 140.7, 144.2, 154.5.

HRMS (ESI-TOF): m/z [M + Na]⁺ calcd for C₂₁H₂₁NO₅S₂Na: 454.0753; found: 454.0755.

***N*-(4-Isopropoxy-3-(phenylsulfonyl)phenyl)-4-methylbenzenesulfonamide (3bv)**

Yellow-white solid; yield: 39.6 mg (89%); mp 168–170 °C.

¹H NMR (400 MHz, CDCl₃): δ = 1.12 (s, 3 H, CHCH₃), 1.13 (s, 3 H, CHCH₃), 2.43 (s, 3 H, ArCH₃), 4.47–4.53 (m, 1 H, CHCH₃), 6.81 (d, J = 8.0 Hz, 1 H, ArH), 7.26–7.28 (m, 3 H, ArH), 7.45–7.53 (m, 3 H, ArH), 7.56–7.61 (m, 4 H, ArH), 7.81 (d, J = 8.0 Hz, 2 H, ArH).

¹³C NMR (100 MHz, CDCl₃): δ = 21.3, 21.7, 71.5, 114.7, 125.0, 127.4, 128.4, 128.5, 128.6, 129.4, 129.8, 131.3, 133.1, 135.6, 141.0, 144.2, 153.6.

HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{22}H_{23}NO_5S_2Na$: 468.0910; found: 468.0911.

Deprotected Compounds 4ba and 4bb

To a solution of **3ba** or **3bb** (1.5 mmol) in dichloromethane (DCM, 10 mL) was added trifluoroacetic acid (6 mmol), and the mixture was refluxed for 6 h, then concentrated under reduced pressure to give a residue which was further purified by flash column chromatography (petroleum ether/EtOAc, 8:1–1:1) to afford compounds **4ba** and **4bb**, respectively.

4-Methoxy-3-(phenylsulfonyl)aniline (4ba)

Yellow-white solid; yield: 375.0 mg (95%); mp 186–188 °C.

1H NMR (400 MHz, $CDCl_3$): δ = 3.66 (s, 3 H, $ArOCH_3$), 6.73–6.75 (m, 1 H, ArH), 6.85–6.87 (m, 1 H, ArH), 7.46–7.58 (m, 4 H, ArH), 7.96 (d, J = 8.0 Hz, 2 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.5, 114.5, 115.9, 121.7, 128.3, 128.5, 129.5, 132.9, 140.1, 141.5, 149.9.

HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{13}H_{13}NO_3SNa$: 286.0508; found: 286.0510.

4-Methoxy-3-((3-nitrophenyl)sulfonyl)aniline (4bb)

Yellow-white solid; yield: 430.0 mg (93%); mp 153–155 °C.

1H NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, $ArOCH_3$), 6.77 (d, J = 8.0 Hz, 1 H, ArH), 6.90–6.92 (m, 1 H, ArH), 7.50 (d, J = 4.0 Hz, 1 H, ArH), 7.71 (t, J = 8.0 Hz, 1 H, ArH), 8.30 (d, J = 8.0 Hz, 1 H, ArH), 8.41–8.44 (m, 1 H, ArH), 8.85 (m, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.5, 114.4, 115.8, 122.6, 124.0, 127.5, 128.0, 129.8, 134.1, 140.4, 143.6, 147.9, 149.7.

HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{13}H_{12}N_2O_5SNa$: 331.0359; found: 331.0360.

N-(4-Methoxy-3-((3-nitrophenyl)sulfonyl)phenyl)acetamide (5)

To a solution of **3bb** (1.5 mmol) in DCM (10 mL) was added trifluoroacetic acid (6 mmol), and the mixture was refluxed for 6 h. Then, the reaction mixture was cooled to room temperature and adjusted to pH 7 by addition of saturated aqueous $NaHCO_3$ solution. The resultant reaction mixture was extracted with DCM and the organic layer was dried with anhydrous Na_2SO_4 , then concentrated under reduced pressure to give a residue. Next, acetic anhydride (1.7 mmol) was added to a solution of this residue in DCM (10 mL), and the mixture was stirred at room temperature for 8 h. Then the reaction mixture was modulated to pH 7 by addition of saturated aqueous $NaHCO_3$ solution and extracted with DCM. Finally, the organic layer was dried with anhydrous Na_2SO_4 , then the solvent was evaporated under reduced pressure.

Yellow-white solid; yield: 446.0 mg (85%); mp 177–179 °C.

1H NMR (400 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, CH_3), 3.80 (s, 3 H, $ArOCH_3$), 6.92 (d, J = 8.0 Hz, 1 H, ArH), 7.73 (t, J = 8.0 Hz, 1 H, ArH), 7.91 (br, 1 H, ArH), 8.01 (s, 1 H, ArH), 8.15 (d, J = 8.0 Hz, 1 H, ArH), 8.30 (d, J = 8.0 Hz, 1 H, ArH), 8.45 (d, J = 8.0 Hz, 1 H, ArH), 8.85 (s, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3, 56.4, 113.3, 121.4, 124.1, 127.2, 127.8, 128.9, 130.0, 131.6, 134.1, 143.0, 148.0, 153.4, 168.8.

HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{15}H_{14}N_2O_6SNa$: 373.0465; found: 373.0466.

N-(4-Hydroxy-3-((3-nitrophenyl)sulfonyl)phenyl)acetamide (6)

Under argon atmosphere, compound **5** (1.0 mmol) and tetrabutylammonium bromide (0.1 mmol) were added to a dried tube and dissolved in anhydrous DCM (5 mL). Then, a 1 M solution of BBr_3 in DCM (4 mL) was slowly added to the reaction mixture at 0 °C, which was stirred at room temperature for 12 h. Subsequently, MeOH was added to the reaction mixture, which was then modulated to pH 7 by addition of saturated aqueous $NaHCO_3$ solution and extracted with DCM. Next, the organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure to give a residue which was purified by flash column chromatography (petroleum ether/EtOAc, 6:1–1:1) to afford compound **6**.

Yellow-white solid; yield: 218.4 mg (65%); mp 155–157 °C.

1H NMR (400 MHz, $CDCl_3$): δ = 2.12 (s, 3 H, CH_3), 6.82 (d, J = 8.0 Hz, 1 H, ArH), 7.62–7.65 (m, 1 H, ArH), 7.81 (t, J = 8.0 Hz, 1 H, ArH), 8.24 (d, J = 4.0 Hz, 1 H, ArH), 8.31–8.33 (m, 1 H, ArH), 8.47–8.50 (m, 1 H, ArH), 8.81 (m, 1 H, ArH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.2, 117.2, 120.6, 123.2, 125.1, 127.4, 128.3, 130.2, 130.8, 133.7, 143.2, 147.9, 152.3, 170.3.

HRMS (ESI-TOF): m/z $[M + Na]^+$ calcd for $C_{14}H_{12}N_2O_6SNa$: 359.0308; found: 359.0310.

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Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0037-1610317>.

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