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Graphic abstract

Ammonium iodide-promoted unprecedented arylsulfonylation of quinone with sodium arylsulfinates

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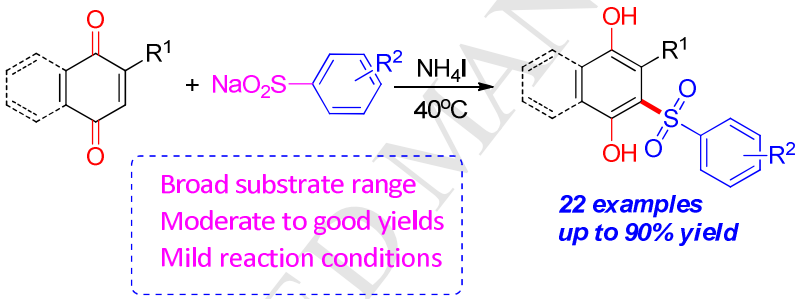
An efficient protocol for the synthesis of quinonyl arylsulfone derivatives has been developed *via* ammonium iodide-promoted arylsulfonylation of quinones with sodium arylsulfinates with moderated to good yields.



Ammonium iodide-promoted unprecedented arylsulfonylation of quinone with sodium arylsulfinates

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Abstract: A novel ammonium iodide-promoted arylsulfonylation of quinones with sodium arylsulfinates has been explored. This reaction proceeded smoothly through unique nucleophilic addition reaction and produced the arylsulfonylation products in moderate to good yields. The reactions proceeded efficiently over a broad range of substrates with good regioselectivity and functional group tolerance.

Key words: quinone; sodium arylsulfinate; ammonium iodide-promoted; nucleophilic addition reaction; arylsulfonylation

1. Introduction

Aryl sulfone skeleton is recognized as a crucial class of scaffold in organic synthesis, medicinal chemistry, and natural products.[1] The development of facile methods for synthesis of aryl sulfones has attracted extensive attention.[2] The traditional routes to access sulfones are oxidation of sulfides and electrophilic sulfonylation of arenes, in which poor functional group compatibility and necessary strong oxidants or strong acids limit its practical application.[3] In recent years, transition metal-catalyzed aromatic C-H bond sulfonylation provided a useful tool for the synthesis of aryl sulfone.[4] However, most of these methods were limited to provide *ortho*-C-H sulfonylation with the assistance of a directing group. Direct sulfonylation *via* C-H functionalization can provide a shortcut for aryl sulfones under metal or metal-free conditions.[5] However, direct sulfonylation of an aromatic C-H bond with less reactive sodium arenesulfinates is rare under metal-free conditions.[6]

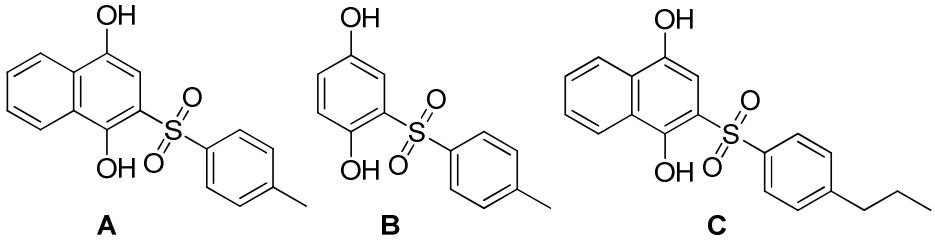


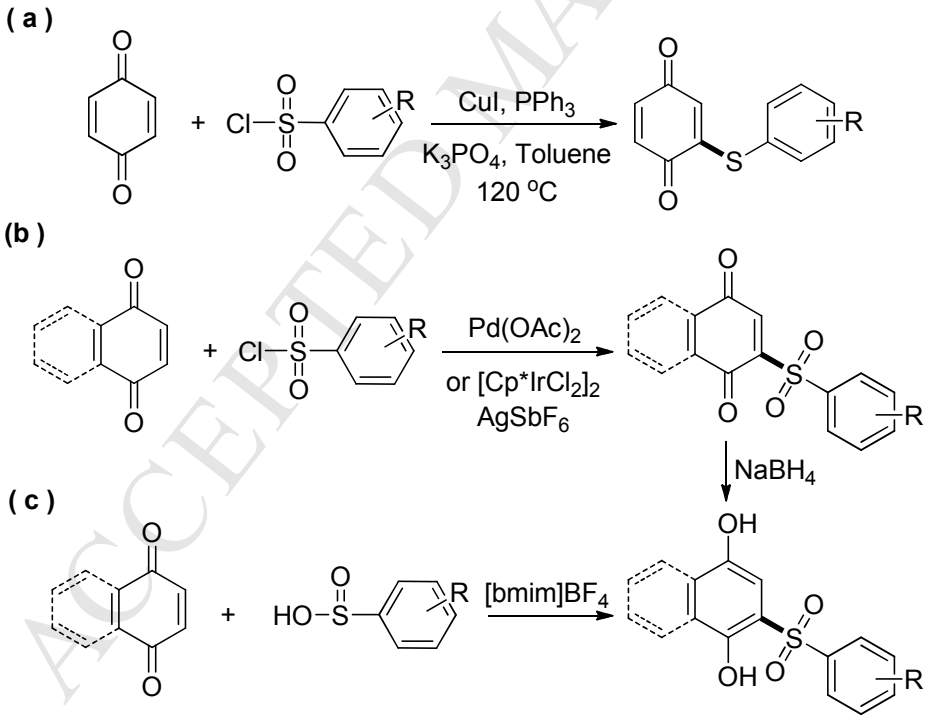
Figure 1. Several FabH inhibitors

As an important cyclic compound, quinone has been found in many natural products, pharmaceuticals and functional materials.[7] Quinonyl aryl sulfone derivatives can be found to be useful skeletons in pharmaceutical as an inhibitor of β-Ketoacyl-ACP-synthase III (FabH), which is a key condensing enzyme in bacterial fatty acid biosynthesis and a part of the dissociated fatty acid synthase (FAS).[8] 2-Tosylnaphthalene-1,4-diol (**A**), 2-tosylbenzene-1,4-diol (**B**) and 2-tosylnaphthalene-1,4-diol (**C**) were identified as potent FabH inhibitors (Figure 1). Their biological evaluation showed that the sulfonyl group and naphthalene-1,4-diol were required for activity against all enzymes.[9] Quinonyl aryl sulfones are generally prepared by oxidation of the corresponding arylthioquinones.[10] In recent years, alternative approaches have been developed for the sulfonylation of quinones using aryl sulfonyl halides or aryl sulfonic acids as sulfonylation reagents through C-H functionalization. In 2016, Wang's group reported the copper and triphenylphosphine-promoted sulfenylation of quinones using arylsulfonyl chlorides as a sulfur source with moderate to good yields (Scheme 1a).[11] Ding and co-workers described a method to prepare arylsulfonyl-quinones and arylsulfonyl-1,4-diols by Pd-catalyzed direct C-sulfone formation by C-S coupling of quinones with sulfonyl chloride; and Huang *et al* developed an efficient method to sylfonyl quinones and sulfonyl-1,4-diols through Ir-catalyzed C-S coupling of quinones with sulfonyl chloride (Scheme 1b).[12] In 2004, Yadav's group disclosed a method of ionic liquids-promoted addition of arylsulfinic acids to quinones to produce the corresponding arylsulfonylhydroquinones, and ionic liquid plays the dual role as the solvent and the catalyst in this reaction (Scheme 1c). [13] Moreover, Bruce et al synthesized a variety of alkyl- or arylsulfonylhydroquinones by the nucleophilic addition of alkyl- or arylsulfinic acids to 1,4-quinones, and the reaction was conducted using a two phase dichloromethane-water system in the presence of trifluoroacetic acid.[14]

Despite these significant advances, almost all of these C-H sulfonylation methods often involved

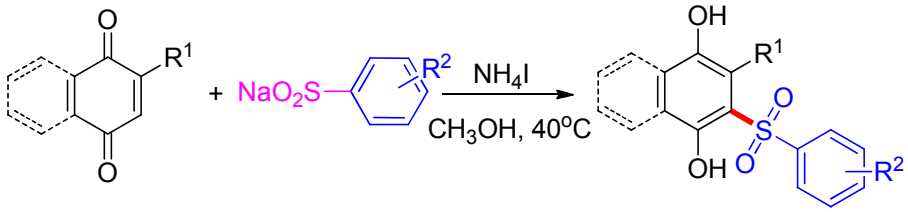
in transition-metal, acid, or base as a catalyst, and required foul-smelling, toxic, and unstable sulfur sources as starting materials, which had lower the synthetic efficiency and generality. As a consequence, it is still an attractive but challenging task to develop a metal-free, environmentally benign method for the rapid and straightforward construction of C-S bonds. Over the past few years, iodine-catalyzed systems have been proven to be powerful tools to form C-S bonds;[15] these systems have been employed in radical and ion reactions. In sharp contrast, iodide catalysts are less explored over the sulfonylation of quinones. Arylsulfinic acid sodium salts are relative stable and moisture-insensitive compared to sulfonyl chlorides. They have been widely used as arylsulfonylation reagents for preparing organosulfonyl compounds.[16] In our continued efforts on the development of new methods for the sulfonylation of quinones, herein, we report an effective route for the sulfonylation of quinones through ammonium iodide-promoted sulfonylation of quinones using sodium sulfinates as the sulfonation reagents (Scheme 1d).

Previous works:



This work:

(d)



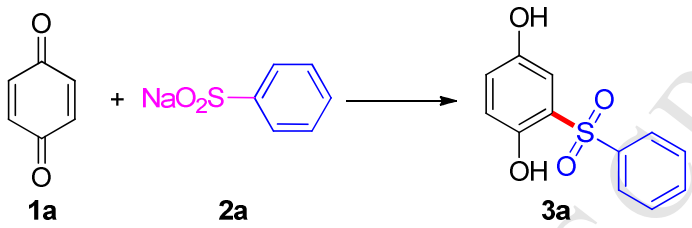
Scheme 1 Synthesis of 2-arylsulfonyl benzene-1,4-diols and naphthalene-1,4-diols

2. Results and discussion

We initiated our investigation on the model reaction of *p*-benzoquinone (**1a**) with sodium benzenesulfinate (**2a**) to optimize the reaction parameters (Table 1). The C2-sulfonylation didn't take place in the absence of any catalysts in DMF at room temperature for 1.0 h (Table 1, entry 1). Inspired by iodide-induced sulfonylation reactions,[15] various additives (4.0 eq.) such as NH_4Cl, NH_4I, $(NH_4)_2SO_4$, KI, I_2, and *tetra*-butylammonium iodide (TBAI) were added for this transformation to improve the yield (Table 1, entries 2-7), and among them NH_4I was found to be the best, and the target product **3a** was afforded in 65% yield (Table 1, entry 3). No desired transformation was observed employing similar ammonium salt $(NH_4)_2SO_4$ (Table 1, entry 4), ruling out the function of NH_4^+ in this reaction. Neither the inorganic KI nor the organic *tertra*-butylammounium (TBAI) did afford the desired product (Table 1, entries 5 and 7), suggesting that iodide anion is not the real form for NH_4I participated in this conversion. When using 4.0 equiv of I_2 instead of NH_4I (Table 1, entry 6), **3a** was not also obtained, which indicated that I_2 was not indeed the actual form to promote this conversion. The additive loading was also investigated, and the result showed that 4.0 eq NH_4I was superior to other loading (Table 1, entries 3, 8-11). It's necessary to use 4.0 eq NH_4I to get satisfactory yield, otherwise the reaction yield decreased to 30% when the additive loading was decreased to 1.0 eq (Table 1, entry 8). The solvent also played an important role in the reaction. Solvents such as H_2O, CH_3CN, dioxane, CH_3OH, DMSO, THF, DCE, and DMF were screened, and CH_3OH was clearly found to be superior to the others (Table 1, entries 3, 12-18), affording **3a** in 70% yield (Table 1, entry 15). The ratio of *p*-benzoquinone with sodium benzenesulfinate was investigated, and the ratio 1:2 of *p*-benzoquinone with sodium benzenesulfinate proved to be the best result, providing 70% yield of **3a** (Supporting information, Table S1, entries 1-4). Subsequently, various reaction temperatures were also examined, and 40 ^oC was found to be the best choice (Table 1, entries 15,

19-21). Finally, the effect of reaction time was also investigated, and good yield could be obtained in 2.0 h (Table 1, entries 19, 22-25). After surveying a variety of additives, additive loadings, solvents, the ratio of reactants, reaction temperatures and times, we found that the combination of the reactant ratio of 1:2 and 4.0 eq NH_4I in CH_3OH at 40 °C for 2.0 h served as the optimal conditions for this transformation.

Table 1 Optimization of reaction conditions[a]



Entry	Additive (eq)	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	-	DMF	25	1.0	trace
2	NH_4Cl (4.0)	DMF	25	1.0	40
3	NH_4I (4.0)	DMF	25	1.0	65
4	$(NH_4)_2SO_4$	DMF	25	1.0	0
5	KI (4.0)	DMF	25	1.0	0
6	I_2 (4.0)	DMF	25	1.0	0
7	TBAI (4.0)	DMF	25	1.0	0
8	NH_4I (1.0)	DMF	25	1.0	30
9	NH_4I (2.0)	DMF	25	1.0	32
10	NH_4I (3.0)	DMF	25	1.0	53
11	NH_4I (5.0)	DMF	25	1.0	55
12	NH_4I (4.0)	H_2O	25	1.0	0
13	NH_4I (4.0)	CH_3CN	25	1.0	0
14	NH_4I (4.0)	dioxane	25	1.0	30
15	NH_4I (4.0)	CH_3OH	25	1.0	70
16	NH_4I (4.0)	DMSO	25	1.0	10
17	NH_4I (4.0)	THF	25	1.0	10

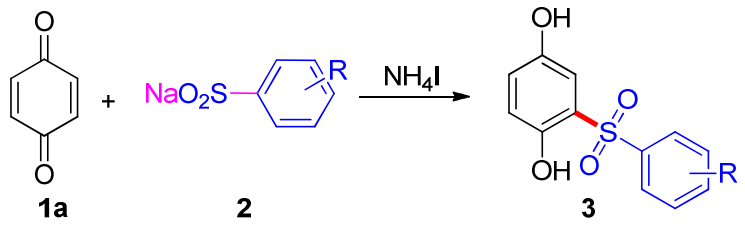
18	NH_4I (4.0)	DCE	25	1.0	0
19	NH_4I (4.0)	CH_3OH	40	1.0	80
20	NH_4I (4.0)	CH_3OH	50	1.0	70
21	NH_4I (4.0)	CH_3OH	60	1.0	65
22	NH_4I (4.0)	CH_3OH	40	0.5	70
23	NH_4I (4.0)	CH_3OH	40	1.5	80
24	NH_4I (4.0)	CH_3OH	40	2.0	85
25	NH_4I (4.0)	CH_3OH	40	2.5	85

[a] Reaction conditions: *p*-benzoquinone **1a** (0.2 mmol, 21.6 mg), sodium phenylsulfinate **2a** (0.4 mmol, 65.6 mg), additive and solvent (3.0 mL).

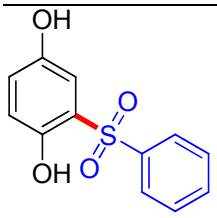
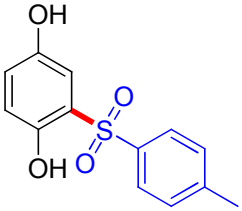
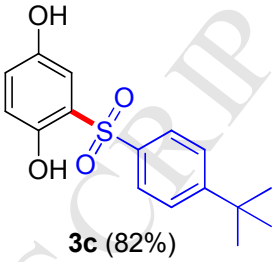
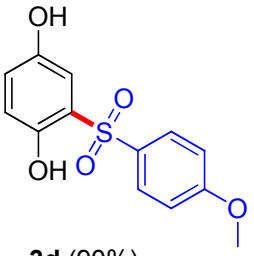
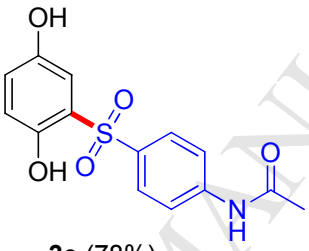
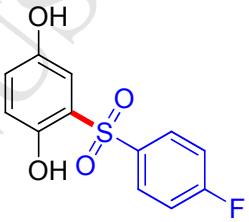
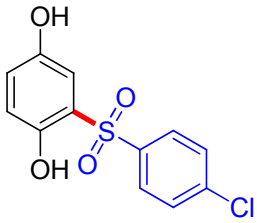
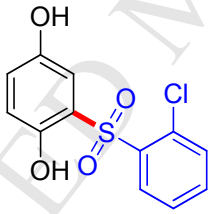
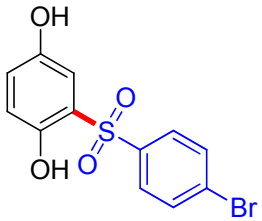
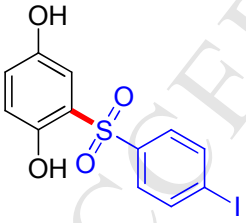
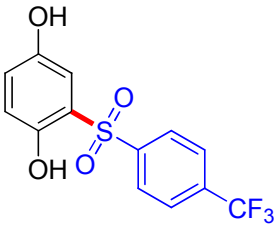
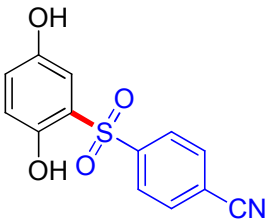
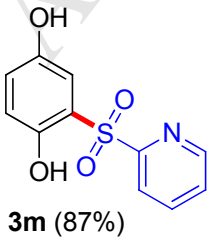
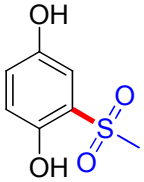
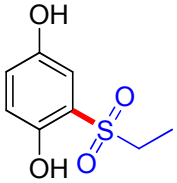
[b] Isolated yield.

With the optimized reaction conditions in hand, we first proceeded to investigate the substrate scope with respect to sodium sulfinates as shown in Table 2. The sulfonylation showed excellent functional group tolerance, and sodium arylsulfinates bearing both electron-donating groups and electron-withdrawing groups could smoothly react with *p*-benzoquinone **1a** to give the desired products (**3a**-**3l**) in good yields (77-90%). To our delight, sodium arylsulfinates with strong withdrawing electron groups such as –F, $–CF_3$, and –CN were well tolerated in this reaction, and the corresponding products (**3f**, **3k** and **3l**) were obtained in 77-83% yields. It was noteworthy that halogen substituents such as fluoro, chloro, bromo, and iodo were well tolerated in this kind of transformation, and the corresponding functionalized products (**3f**, **3g**-**3j**) could be used as substrates for further functionalization. In addition, heteroaromatic sulfinate proceeded smoothly to afford the target product (**3m**) in good yield (87%). Gratifyingly, the sodium aliphatic sulfinates could also be used as viable substrates to afford the corresponding sulfones (**3n** and **3o**) in good yields (84% and 85%). A single crystal of **3d** was obtained from trichloromethane. Its crystal structure (Fig. 1) exhibited that C2 of *p*-benzoquinone was arylsulfonylated by NH_4I-promoted direct functionalization, and two carbonyl groups of *p*-benzoquinone were transformed into two hydroxyl groups. CCDC 1563390 for **3d** contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

Table 2 Substrate scope of sodium sulfinates [a,b]



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

 **3a** (85%)	 **3b** (83%)	 **3c** (82%)
 **3d** (90%)	 **3e** (78%)	 **3f** (83%)
 **3g** (80%)	 **3h** (79%)	 **3i** (85%)
 **3j** (88%)	 **3k** (77%)	 **3l** (82%)
 **3m** (87%)	 **3n** (84%)	 **3o** (85%)

[a] Reaction conditions: *p*-benzoquinone **1a** (0.2 mmol, 21.6 mg), sodium arylsulfinate **2** (0.4 mmol), and NH_4I (0.8 mmol, 116 mg) in 3.0 mL CH_3OH solvent, 40 °C for 2.0 h.

[b] Isolated yield.

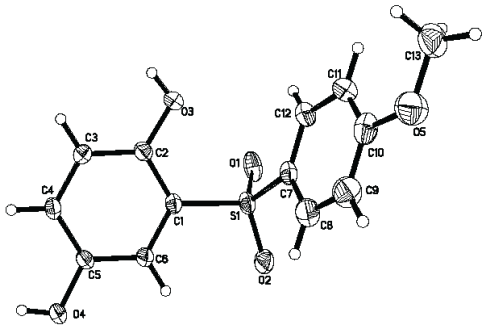
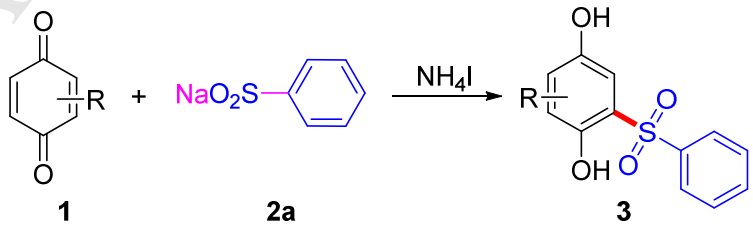
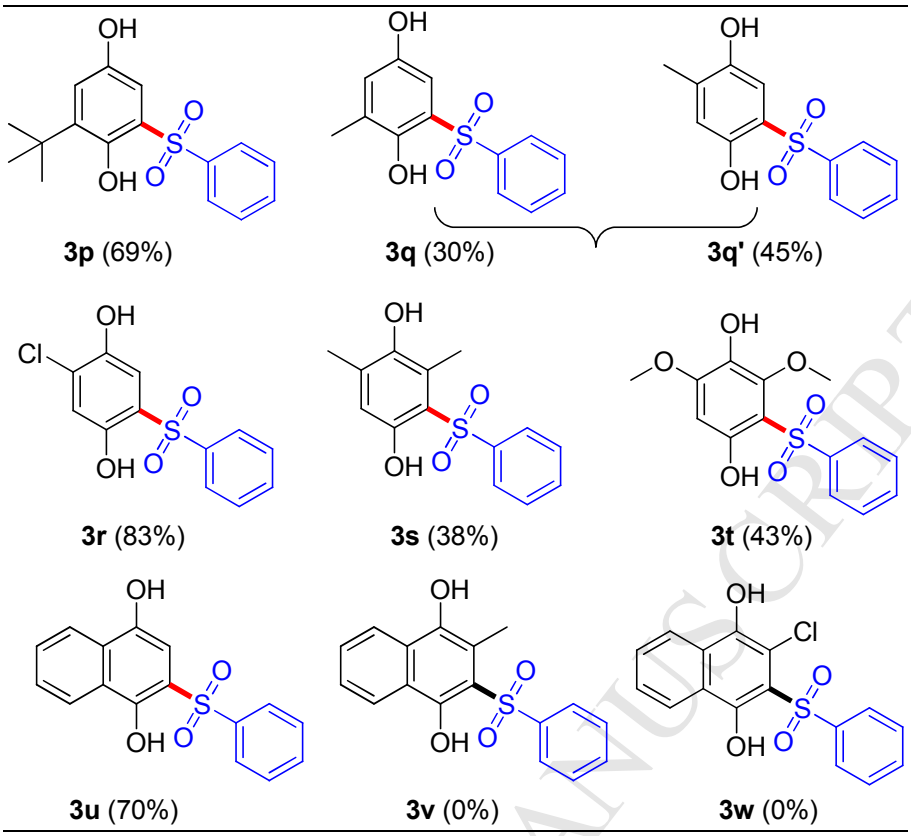


Figure 2. Single crystal structure of **3d**

After screening various sodium sulfinates, we next sought to expand the scope of different substituted quinones under the standard reaction conditions (Table 3). The results demonstrated that *p*-benzoquinones bearing electron-donating and -withdrawing groups were both well tolerated in this reaction, and the desired products could be obtained in moderate to good yields (**3p**-**3t**). When 2-methylcyclohexa-2,5-diene-1,4-dione was employed, two isomers were obtained in a combination yield of 75% (**3q** : **3q′** = 1 : 1.5). The different substituent position in *p*-benzoquinone profoundly affected the reaction yield. When 2,5-disubstituted *p*-benzoquinones were employed, the yields of corresponding products were clearly decreased even after an extended reaction time (**3s** and **3t**), possibly due to the steric interference. To our delight, naphthalene-1,4-dione could also produce the desired product in a moderate yield (**3t**). Unfortunately, 2-substituted naphthalene-1,4-diones such as 2-chloronaphthalene-1,4-dione and 2-methylnaphthalene-1,4-dione failed to give the corresponding products under the current reaction conditions (**3v** and **3w**), which was presumably attributed to the influence of the steric hindrance and low reactivity of C3 position.

Table 3 Substrate scope of quinones [a,b]

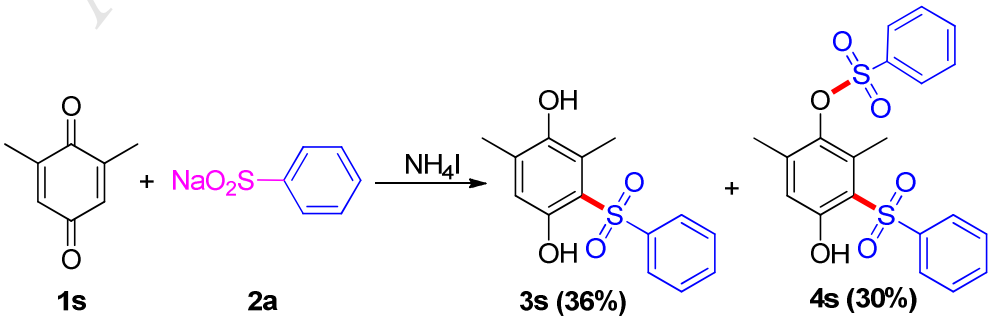




[a] Reaction conditions: quinones **1** (0.2 mmol), sodium phenylsulfinate **2a** (0.4 mmol, 65.6 mg), and NH_4I (0.8 mmol, 116 mg) in 3.0 mL CH_3OH solvent, 40 ^oC for 2.0 h.

[b] Isolated yield.

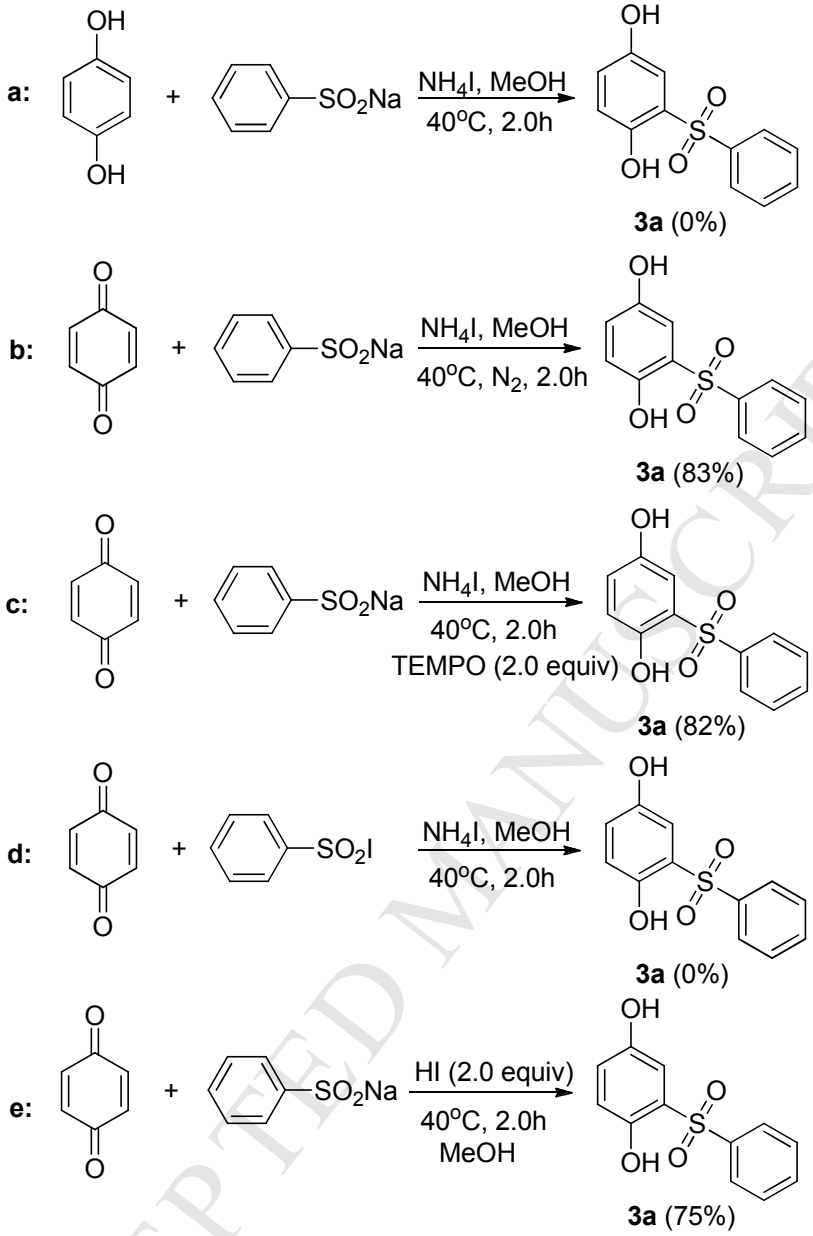
To further explore the utility of this method, the synthesis of bisarylsulfonylated quinone derivatives was also investigated. Herein, we further examined the reaction of 2,6-dimethylcyclohexa-2,5-diene-1,4-dione (**1s**) and sodium phenylsulfinate (**2a**) using NH_4I-promoted this transformation. The reaction temperature was increased to 60 ^oC, and the reaction time was also prolonged to 5.0 h. Interestingly, the result showed that 2,6-dimethyl-3,5-bis(phenylsulfonyl)benzene-1,4-diol was not obtained, and two products were provided in a combination yield of 66 % (**3s** : **4s** = 1.2 : 1). The structure of **4s** was elucidated by HR MS, IR, and NMR.



Scheme 2 Synthesis diarylsulfonyl hydroxybenzene derivatives

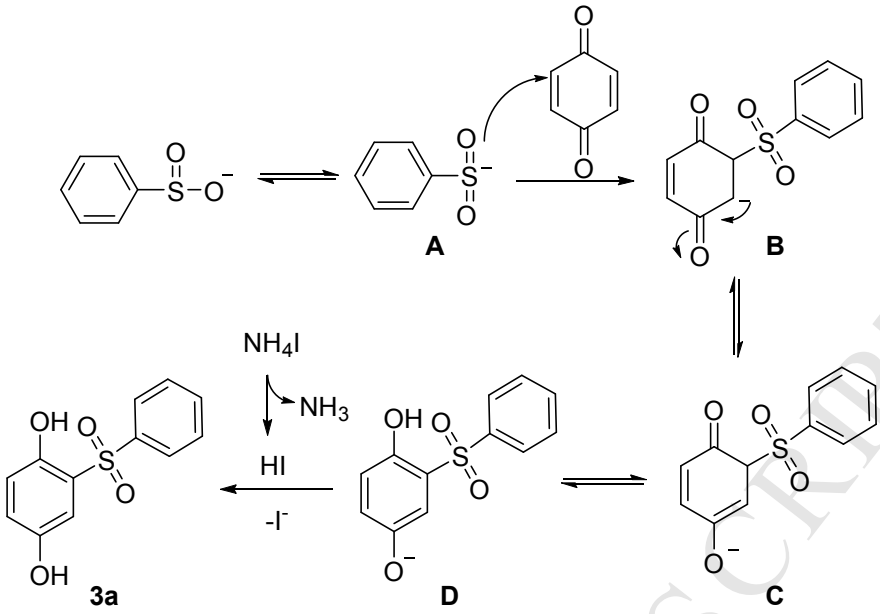
Reaction conditions: 2,6-dimethylcyclohexa-2,5-diene-1,4-dione **1S** (0.2 mmol, 27.2 mg), sodium phenylsulfinate **2a** (0.4 mmol, 65.6 mg), and NH_4I (0.8 mmol, 116 mg) in 3.0 mL CH_3OH solvent, 60 ^oC for 5.0 h.

To investigate the reaction mechanism, a series of control experiments were conducted (Scheme 3). When hydroquinone was employed, the reaction failed to deliver the desired product **3a** under standard conditions which revealed that the NH_4I-promoted sulfonylation of quinones were not an electrophilic substitution reaction (Scheme 3a). Under the protection of N_2, the target product **3a** could be obtained in a good yield, indicating that the oxygen atom of sulfone group in **3a** does not come from O_2 (Scheme 3b). Moreover, when a radical inhibitor 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) was added to the reaction, the yield of the desired product **3a** was decreased slightly, and the formation of **3a** was not suppressed, which indicated that the sulfonylation was not involved in a radical reaction (Scheme 3c). In addition, when benzenesulfonyl iodine was employed as a sulfonylation source, the reaction didn't proceed under the standard conditions. The result suggested that benzenesulfonyl iodine was not a reactive intermediate (Scheme 3d). Interestingly, when using 2.0 equiv of HI instead of 4.0 equiv of NH_4I, **3a** was obtained with 75% yield, which suggested that HI was indeed the actual form to promote this conversion (Scheme 3e). When phenylsulfinic acid and *p*-quinone were employed as reaction materials in the absence of ammonium iodide, we found that the desired product was given with poor yield (57%) even after long reaction time (4.0 h). When ammonium iodide was added, the quinones exhibit enhanced reactivity thereby reducing the reaction times and improving the yields significantly. The use of ammonium iodide for this transformation helps to avoid the use of corrosive acids as promoters, thereby minimizing the production of acid waste during workup.



Scheme 3 Control experiments

Although the exact mechanism for this sulfonylation reaction was still unclear at this stage, based on the above investigations and literature precedents,[13, 17] a plausible mechanism is proposed and depicted in Scheme 4. Initially, a sulfur centered anion **A** generated by the resonation of phenylsulfinate anion, followed by nucleophilic addition to *p*-benzoquinone **1a**. This leads to the formation of intermediate **B**. The intermediate **C** is provided by the resonation of **B**. Subsequently, **C** may undergo a tautomerization to give the intermediate **D**. Ammonium iodide is decomposed into a hydroiodic acid and an ammonia. Finally, the intermediate **D** including an oxygen centered anion links with a proton to give the desired product **3a**.



Scheme 4 Proposed reaction mechanism

3. Conclusion

In summary, we have developed an efficient and practical method for the preparation of 2-arylsulfonyl quinone derivatives based on ammonium iodide-promoted reaction of quinone with sodium arylsulfinates. This reaction initiated *via* an arylsulfonyl anion generated from a salt arylsulfinate rather than the arylsulfonyl radical. A plausible reaction mechanism has been given on the basis of the control experiments.

4. Experimental

4.1 General information

All substrates purchased from *J* & *K* Scientific Ltd. were used without further purification. Column chromatography was performed using 300-400 mesh silica with the indicated solvent system according to standard techniques. Nuclear magnetic resonance spectra were recorded on Bruker Avance 400 MHz spectrometer. Chemical shifts for ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and br = broad), coupling constant in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane. High resolution mass spectra (HR MS) were obtained on Thermo Scientific LTQ Orbitrap XL instrument using the ESI technique. IR spectra were recorded on Shimadazu IR-408 Fourier transform infrared spectrophotometer using a thin film supported on KBr pellets. Melting

points were measured on an XT4A microscopic apparatus uncorrected.

4.2 General experimental procedure for the synthesis of arylsulfonylated quinone derivatives (3)

Quinone **1** (0.2 mmol), sodium arylsulfinate **2** (0.4 mmol), and NH_4I (0.8mmol, 116 mg) in methanol (3.0 mL) were added to a 25 mL Schlenk tube. The mixture was heated at 40 ^oC for 2.0 h (monitored by TLC). After completion of the reaction, the solvent was distilled under vacuum. 10 mL ethyl acetate was added to the residuum, and 20 mL saturated sodium chloride solution washed two times. The organic phase was dried over anhydrous $NaSO_4$ and concentrated under vacuum. The crude product was purified by silica gel column chromatography to give the desired products **3** using ethyl acetate/petroleum ether (1:5 to 1:1) as eluant.

*4.2.1. 2-(Phenylsulfonyl)benzene-1,4-diol (**3a**)*

Light yellow solid, mp 197-198 ^oC [lit[13] mp 193 ^oC]. IR (KBr) ν(cm^{-1}): 3294, 1508, 1462, 1369, 1288, 1223, 1142, 1088. ^1H NMR (400 MHz, DMSO) δ: 9.97 (bs, 1H), 9.42 (bs, 1H), 7.89 (dd, J_{H-H} = 7.2 Hz, J_{H-H} = 1.4 Hz, 2H), 7.66-7.62 (m, 1H), 7.58-7.54 (m, 2H), 7.34 (d, J_{H-H} = 3.0 Hz, 1H), 6.92 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.74 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 149.9, 148.6, 141.7, 133.5 (CH), 129.2 (CH), 128.2 (CH), 126.4, 123.3 (CH), 118.9 (CH), 116.1 (CH), 114.2 (CH). HR MS (ESI) m/z: 251.0375 $[M + H]^+$ (calcd for $C_{12}H_{11}O_4S^+$ 251.0373).

*4.2.2. 2-Tosylbenzene-1,4-diol (**3b**)*

Yellow solid, mp 184-185 ^oC [lit[13] mp 211-212 ^oC]. IR (KBr) ν(cm^{-1}): 3282, 1593, 1504, 1458, 1365, 1284, 11242, 1138, 1080. ^1H NMR (400 MHz, DMSO) δ: 9.91 (bs, 1H), 9.38 (bs, 1H), 7.77 (d, J_{H-H} = 8.2 Hz, 2H), 7.36-7.32 (m, 3H), 6.90 (dd, J_{H-H} = 8.7 Hz, J_{H-H} = 3.0 Hz, 1H), 6.73 (d, J_{H-H} = 8.7 Hz, 1H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 149.9, 148.6, 144.0, 138.9, 129.7 (CH), 128.3 (CH), 126.8, 123.1 (CH), 118.9 (CH), 114.2 (CH), 21.5 (CH_3). HR MS (ESI) m/z: 265.0531 $[M + H]^+$ (calcd for $C_{13}H_{13}IO_4S^+$ 265.0529).

*4.2.3. 2-((4-(tert-Butyl)phenyl)sulfonyl)benzene-1,4-diol (**3c**)*

Light yellow solid, mp 165-167 ^oC. IR (KBr) ν(cm^{-1}): 3259, 1962, 1597, 1512, 1361, 1281, 1142, 1107. ^1H NMR (400 MHz, DMSO) δ: 9.94 (bs, 1H), 9.40 (bs, 1H), 7.84 (d, J_{H-H} = 8.5 Hz, 2H), 7.57 (d, J_{H-H} = 8.5 Hz, 2H), 7.37-7.36 (m, 1H), 6.93 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.76 (d, J_{H-H} = 8.8 Hz, 1H), 1.24 (s, 9H). ^{13}C NMR (100 MHz, DMSO) δ: 156.6, 149.9, 148.6, 139.0, 128.2 (CH), 126.8, 126.1 (CH), 123.2 (CH), 119.0 (CH), 114.4 (CH), 35.2, 31.2 (CH_3). HR MS (ESI) m/z: 307.0999 $[M + H]^+$ (calcd for $C_{16}H_{19}O_4S^+$ 307.0999).

*4.2.4 2-((4-Methoxyphenyl)sulfonyl)benzene-1,4-diol (**3d**)*

Light yellow solid, mp 190-191 °C [lit[18] mp 188-189 °C]. IR (KBr) ν(cm^{-1}): 3259, 1593, 1500, 1365, 1273, 1134, 1092. ^{1}H NMR (400 MHz, DMSO) δ: 9.90 (bs, 1H), 9.39 (bs, 1H), 7.85 (d, J_{H-H} = 8.9 Hz, 2H), 7.34 (d, J_{H-H} = 3.0 Hz, 1H), 7.08 (d, J_{H-H} = 8.9 Hz, 2H), 6.91 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.75 (d, J_{H-H} = 8.8 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 167.9, 154.6, 153.2, 138.0, 135.4 (CH), 132.0, 127.7 (CH), 123.7 (CH), 119.2 (CH), 118.9 (CH), 60.8 (CH_3). HR MS (ESI) m/z: 281.0478 $[M + H]^+$ (calcd for $C_{13}H_{13}ClO_5S^+$ 281.0478).

*4.2.5. N-(4-((2,5-Dihydroxyphenyl)sulfonyl)phenyl)acetamide (**3e**)*[19]

Wine red solid, mp 281-282 °C. IR (KBr) ν(cm^{-1}): 3344, 3194, 1678, 1593, 1543, 1504, 1358, 1284, 1261, 1146, 1092. ^{1}H NMR (400 MHz, DMSO) δ: 10.3 (s, 1H), 9.85 (bs, 1H), 9.32 (bs, 1H), 7.81 (d, J_{H-H} = 8.8 Hz, 2H), 7.73 (d, J_{H-H} = 8.8 Hz, 2H), 7.29 (d, J_{H-H} = 3.0 Hz, 1H), 6.88 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.71 (d, J_{H-H} = 8.8 Hz, 1H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 169.5, 149.8, 148.5, 143.8, 135.3, 129.6 (CH), 127.1, 123.0 (CH), 118.9 (CH), 118.6 (CH), 114.2 (CH), 24.5 (CH_3). HR MS (ESI) m/z: 308.0589 $[M + H]^+$ (calcd for $C_{14}H_{14}NO_5S^+$ 308.0587).

*4.2.6. 2-((4-Fluorophenyl)sulfonyl)benzene-1,4-diol (**3f**)*

White solid, mp 199-200 °C. IR (KBr) ν(cm^{-1}): 3275, 1597, 1504, 1458, 1365, 1277, 1138, 1080. ^{1}H NMR (400 MHz, DMSO) δ: 10.03 (bs, 1H), 9.42 (bs, 1H), 7.98-7.94 (m, 2H), 7.43-7.38 (m, 2H), 7.32 (d, J_{H-H} = 3.0 Hz, 1H), 6.92 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.74 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 166.3, 163.8, 138.0 (d, J_{F-C} = 2.7 Hz), 131.5 (d, J_{F-C} = 9.7 Hz) (CH), 126.3, 123.4 (CH), 119.0 (CH), 116.4 (d, J_{F-C} = 22.6 Hz) (CH), 114.1 (CH). ^{19}F NMR (376 MHz, DMSO) δ: -105.7. HR MS (ESI) m/z: 269.0281 $[M + H]^+$ (calcd for $C_{12}H_{10}FO_4S^+$ 269.0278).

*4.2.7. 2-((4-Chlorophenyl)sulfonyl)benzene-1,4-diol (**3g**)*

Light yellow solid, mp 208-209 °C [lit[20] mp 210-212 °C]. IR (KBr) ν(cm^{-1}): 3267, 1504, 1458, 1365, 1296, 1277, 1215, 1142, 1088. ^{1}H NMR (400 MHz, DMSO) δ: 10.05 (bs, 1H), 9.43 (bs, 1H), 7.88 (dd, J_{H-H} = 6.8 Hz, J_{H-H} = 1.8 Hz, 2H), 7.64 (dd, J_{H-H} = 6.8 Hz, J_{H-H} = 1.8 Hz, 2H), 7.31 (d, J_{H-H} = 3.0 Hz, 1H), 6.93 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.74 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 149.9, 148.6, 140.6, 138.6, 130.2 (CH), 129.4 (CH), 126.0, 123.6 (CH), 119.0 (CH), 114.2 (CH). HR MS (ESI) m/z: 284.9986 $[M + H]^+$ (calcd for $C_{12}H_{10}ClO_4S^+$ 284.9983).

*4.2.8. 2-((2-Chlorophenyl)sulfonyl)benzene-1,4-diol (**3h**)*

White solid, mp 212-213 °C. IR (KBr) ν(cm^{-1}): 3294, 1500, 1446, 1346, 1300, 1149, 1126. ^{1}H NMR

(400 MHz, DMSO) δ: 9.87 (bs, 1H), 9.41 (bs, 1H), 8.22 (dd, J_{H-H} = 7.7 Hz, J_{H-H} = 1.7 Hz, 1H), 7.68-7.59 (m, 2H), 7.56 (dd, J_{H-H} = 7.7 Hz, J_{H-H} = 1.2 Hz, 1H), 7.37 (d, J_{H-H} = 3.0 Hz, 1H), 6.94 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.70 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 149.6, 148.6, 138.9, 135.2 (CH), 132.4 (CH), 131.8 (CH), 131.2, 127.8 (CH), 125.2, 123.7 (CH), 118.7 (CH), 115.4 (CH). HR MS (ESI) m/z: 284.9979 $[M + H]^+$ (calcd for $C_{12}H_{10}ClO_4S^+$ 284.9983).

*4.2.9. 2-((4-Bromophenyl)sulfonyl)benzene-1,4-diol (**3i**)*

Light yellow solid, mp 216-217 °C. IR (KBr) ν(cm^{-1}): 3275, 1570, 1512, 1466, 1365, 1300, 1269, 1215, 1134, 1088. ^{1}H NMR (400 MHz, DMSO) δ: 10.07 (bs, 1H), 9.46 (bs, 1H), 7.83 (d, J_{H-H} = 8.7 Hz, 2H), 7.76 (d, J_{H-H} = 8.7 Hz, 2H), 7.38 (d, J_{H-H} = 3.0 Hz, 1H), 6.97 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.79 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 150.0, 148.7, 141.0, 132.4 (CH), 130.3 (CH), 127.6, 126.0, 123.7 (CH), 119.1 (CH), 116.2 (CH), 114.2 (CH). HR MS (ESI) m/z: 328.9473 $[M + H]^+$ (calcd for $C_{12}H_{10}BrO_4S^+$ 328.9478).

*4.2.10. 2-((4-Iodophenyl)sulfonyl)benzene-1,4-diol (**3j**)*

Light yellow solid, mp 215-216 °C. IR (KBr) ν(cm^{-1}): 3267, 1562, 1512, 1469, 1373, 1296, 1265, 1215, 1142. ^{1}H NMR (400 MHz, DMSO) δ: 10.03 (bs, 1H), 9.44 (bs, 1H), 7.96 (d, J_{H-H} = 8.5 Hz, 2H), 7.64 (d, J_{H-H} = 8.5 Hz, 2H), 7.33 (d, J_{H-H} = 3.0 Hz, 1H), 6.94 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.76 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 150.0, 148.7, 141.4, 138.2 (CH), 130.0 (CH), 126.0, 123.6 (CH), 119.0 (CH), 114.2 (CH), 102.0. HR MS (ESI) m/z: 376.9334 $[M + H]^+$ (calcd for $C_{12}H_{10}IO_4S^+$ 376.9339).

*4.2.11. 2-((4-(Trifluoromethyl)phenyl)sulfonyl)benzene-1,4-diol (**3k**)*

White solid, mp 172-173 °C. IR (KBr) ν(cm^{-1}): 3417, 3194, 1504, 1462, 1400, 1323, 1273, 1142, 1122, 1061. ^{1}H NMR (400 MHz, DMSO) δ: 10.14 (bs, 1H), 9.50 (bs, 1H), 8.12 (d, J_{H-H} = 8.2 Hz, 2H), 7.94 (d, J_{H-H} = 8.4 Hz, 2H), 7.40 (d, J_{H-H} = 3.0 Hz, 1H), 6.98 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.79 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 149.4 (d, J_{F-C} = 129.8 Hz), 145.6, 133.2 (q, J_{F-C} = 31.9 Hz), 129.2 (CH), 126.4 (d, J_{F-C} = 3.6 Hz) (CH), 125.5, 124.0 (CH), 123.8 (d, J_{F-C} = 271.3 Hz), 119.1 (CH), 116.1 (CH), 114.2 (CH). ^{19}F NMR (376 MHz, DMSO) δ: -61.8. HR MS (ESI) m/z: 319.0247 $[M + H]^+$ (calcd for $C_{13}H_{10}F_3O_4S^+$ 319.0246).

*4.2.12. 4-((2,5-Dihydroxyphenyl)sulfonyl)benzonitrile (**3l**)*

Light yellow solid, mp 175-176 °C [lit[21] mp 182-183 °C]. IR (KBr) ν(cm^{-1}): 3252, 1496, 1466, 1392, 1311, 1277, 1233, 1142. ^{1}H NMR (400 MHz, DMSO) δ: 10.17 (bs, 1H), 9.50 (bs, 1H), 8.07-8.02 (m,

4H), 7.32 (d, J_{H-H} = 2.9 Hz, 1H), 6.95 (dd, J_{H-H} = 8.7 Hz, J_{H-H} = 2.9 Hz, 1H), 6.75 (d, J_{H-H} = 8.7 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 150.0, 148.8, 145.7, 133.4 (CH), 129.0 (CH), 125.1, 124.1 (CH), 119.0 (CH), 118.1, 115.9, 114.2 (CH). HR MS (ESI) m/z: 276.0323 $[M + H]^+$ (calcd for $C_{13}H_{10}NO_4S^+$ 276.0325).

*4.2.13. 2-(pyridin-2-ylsulfonyl)benzene-1,4-diol (**3m**)*

Yellow solid, mp 154-155 °C. IR (KBr) ν(cm^{-1}): 3444, 3012, 1468, 1431, 1234, 1086, 1024. ^{1}H NMR (400 MHz, DMSO) δ: 9.87 (bs, 1H), 9.45 (bs, 1H), 8.63 (d, J_{H-H} = 4.4 Hz, 1H), 8.20 (d, J_{H-H} = 7.8 Hz, 1H), 8.12 (m, 1H), 7.67-7.64 (m, 1H), 7.38 (d, J_{H-H} = 3.0 Hz, 1H), 6.97 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 3.0 Hz, 1H), 6.75 (d, J_{H-H} = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 158.8, 150.3 (CH), 149.9, 148.8, 138.8 (CH), 127.8 (CH), 124.6, 123.6 (CH), 122.9 (CH), 118.7 (CH), 115.2 (CH). HR MS (ESI) m/z: 252.0327 $[M + H]^+$ (calcd for $C_{11}H_{10}NO_4S^+$ 252.0325).

*4.2.14. 2-(Methylsulfonyl)benzene-1,4-diol (**3n**)*

Light yellow solid, mp 112-113 °C [lit[22] mp 121-124 °C]. IR (KBr) ν(cm^{-1}): 3346, 3014, 2931, 1518, 1450, 1286, 1196, 1142. ^{1}H NMR (400 MHz, DMSO) δ: 10.05 (bs, 1H), 9.44 (bs, 1H), 7.12 (d, J_{H-H} = 2.9 Hz, 1H), 6.92 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 2.9 Hz, 1H), 6.87 (d, J_{H-H} = 8.8 Hz, 1H), 3.20 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 149.9, 148.4, 126.9, 122.7 (CH), 118.8 (CH), 113.8 (CH), 42.7 (CH_3). HR MS (ESI) m/z: 189.0219 $[M + H]^+$ (calcd for $C_7H_9O_4S^+$ 189.0216).

*4.2.15. 2-(Ethylsulfonyl)benzene-1,4-diol (**3o**)*

Light yellow solid, mp 94-95 °C. IR (KBr) ν(cm^{-1}): 3346, 3064, 2987, 1504, 1454, 1340, 1300, 1263, 1223, 1122, 1049. ^{1}H NMR (400 MHz, DMSO) δ: 9.76 (bs, 2H), 7.10 (d, J_{H-H} = 2.9 Hz, 1H), 6.93 (dd, J_{H-H} = 8.8 Hz, J_{H-H} = 2.9 Hz, 1H), 6.87 (d, J_{H-H} = 8.8 Hz, 1H), 3.34 (q, J_{H-H} = 7.4 Hz, 2H), 1.06 (t, J_{H-H} = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 149.9, 148.6, 124.3, 122.8 (CH), 118.8 (CH), 114.8 (CH), 47.9 (CH_2), 7.4 (CH_3). HR MS (ESI) m/z: 203.0375 $[M + H]^+$ (calcd for $C_8H_{11}O_4S^+$ 203.0373).

*4.2.16. 2-(tert-Butyl)-6-(phenylsulfonyl)benzene-1,4-diol (**3p**)*

Colorless solid, mp 185-186 °C. IR (KBr) ν(cm^{-1}): 3467, 3285, 1476, 1445, 1273, 1235, 1195. ^{1}H NMR (400 MHz, DMSO) δ: 9.49 (bs, 1H), 8.77 (bs, 1H), 7.94 (d, J_{H-H} = 8.7 Hz, 2H), 7.73-7.69 (m, 1H), 7.67-7.61 (m, 2H), 7.04 (d, J_{H-H} = 3.0 Hz, 1H), 6.96 (d, J_{H-H} = 3.0 Hz, 1H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, DMSO) δ: 150.7, 146.8, 142.0, 141.6, 134.3 (CH), 130.0 (CH), 127.3 (CH), 126.9, 121.8 (CH), 111.4 (CH), 35.4, 29.7 (CH_3). HR MS (ESI) m/z: 307.1002 $[M + H]^+$ (calcd for $C_{16}H_{19}O_4S^+$ 307.0999).

*4.2.17. 2-Methyl-6-(phenylsulfonyl)benzene-1,4-diol (**3q**)*

Colorless solid, mp 182-183 °C [lit[23] mp 177.9-179.8 °C]. IR (KBr) ν(cm^{-1}): 3464, 3286, 1473, 1442, 1284, 1223, 1192, 1142, 1122, 1072. ^{1}H NMR (400 MHz, DMSO) δ: 9.40 (bs, 1H), 8.88 (bs, 1H), 7.89 (d, J_{H-H} = 7.5 Hz, 2H), 7.67-7.64 (m, 1H), 7.60-7.56 (m, 2H), 7.18 (d, J_{H-H} = 2.8 Hz, 1H), 6.85 (d, J_{H-H} = 2.8 Hz, 1H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 150.3, 146.2, 142.0, 133.6 (CH), 129.8, 129.4 (CH), 128.2, 128.0 (CH), 124.4 (CH), 111.9 (CH), 16.7 (CH_3). HR MS (ESI) m/z: 265.0532 $[M + H]^+$ (calcd for $C_{13}H_{13}O_4S^+$ 265.0529).

*4.2.18. 2-Methyl-5-(phenylsulfonyl)benzene-1,4-diol (**3q'**)*

Colorless solid, mp 173-174 °C [lit[23] mp 186.5-187.3 °C]. IR (KBr) ν(cm^{-1}): 3425, 3279, 1523, 1454, 1415, 1369, 1277, 1192,1138,1084. ^{1}H NMR (400 MHz, DMSO) δ: 9.84 (bs, 1H), 9.36 (bs, 1H), 7.88 (d, J_{H-H} = 7.3 Hz, 2H), 7.63-7.60 (m, 1H), 7.57-7.53 (m, 2H), 7.37 (s, 1H), 6.64 (s, 1H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 148.4, 148.1, 142.2, 133.7, 133.3 (CH), 129.2 (CH), 128.0 (CH), 123.6, 119.8 (CH), 113.5 (CH), 16.7 (CH_3). HR MS (ESI) m/z: 265.0533 $[M + H]^+$ (calcd for $C_{13}H_{13}O_4S^+$ 265.0529).

*4.2.19. 2-Chloro-3-(phenylsulfonyl)benzene-1,4-diol (**3r**)*

Colorless solid, mp 163-165 °C. IR (KBr) ν(cm^{-1}): 3424, 3232, 1459, 1432, 1257. ^{1}H NMR (400 MHz, DMSO) δ: 10.26 (bs, 2H), 7.89 (d, J_{H-H} = 7.7 Hz, 2H), 7.67-7.63 (m, 1H), 7.61-7.55 (m, 3H), 6.88 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 148.6, 145.9, 141.3, 133.7 (CH), 129.3 (CH), 128.2 (CH), 127.1, 125.7, 118.8 (CH), 115.6 (CH). HR MS (ESI) m/z: 284.9985 $[M + H]^+$ (calcd for $C_{12}H_{10}ClO_4S^+$ 284.9983).

*4.2.20. 3,5-Dimethyl-2-(phenylsulfonyl)benzene-1,4-diol (**3s**)*

Colorless solid, mp 146-147 °C [lit[13] mp 146 °C]. IR (KBr) ν(cm^{-1}): 3421, 3224, 1616, 1570, 1473, 1442, 1346, 1377, 1219, 1126, 1088. ^{1}H NMR (400 MHz, DMSO) δ: 9.75 (bs, 1H), 8.12 (bs, 1H), 7.84 (d, J_{H-H} = 7.4 Hz, 2H), 7.65 (t, J_{H-H} = 7.3 Hz, 1H), 7.57 (t, J_{H-H} = 7.2 Hz, 2H), 6.60 (s, 1H), 2.39 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 150.6, 146.6, 143.5, 135.3, 133.5 (CH), 129.4 (CH), 126.9 (CH), 125.9, 121.0, 117.3 (CH), 17.7 (CH_3), 13.6 (CH_3). HR MS (ESI) m/z: 279.0685 $[M + H]^+$ (calcd for $C_{14}H_{15}O_4S^+$ 279.0686).

*4.2.21. 3,5-Dimethoxy-2-(phenylsulfonyl)benzene-1,4-diol (**3t**)*

Colorless solid, mp 139-140 °C. IR (KBr) ν(cm^{-1}): 3471, 3375, 3278, 2943, 1616, 1577, 1500, 1442, 1373, 1300, 1192, 1153, 1092, 1057. ^{1}H NMR (400 MHz, DMSO) δ: 9.70 (bs, 1H), 7.88 (d, J_{H-H} = 7.3

Hz, 2H), 7.68-7.65 (m, 1H), 7.61-7.57 (m, 2H), 6.37 (s, 1H), 3.81 (s, 3H), 3.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 154.4, 149.2, 143.3, 143.1, 133.8 (CH), 129.5 (CH), 127.1 (CH), 124.8, 109.3, 97.0 (CH), 59.8 (CH_3), 56.4 (CH_3). HR MS (ESI) m/z: 311.0586 $[M + H]^+$ (calcd for $C_{14}H_{15}O_6S^+$ 311.0584).

*4.2.22. 2-(Phenylsulfonyl)naphthalene-1,4-diol (**3u**)*

Deep yellow solid, mp 166-167 °C [lit[13] mp 178 °C]. IR (KBr) ν(cm^{-1}): 3321, 1577, 1446, 1277, 1126, 1088. ^{1}H NMR (400 MHz, DMSO) δ: 10.21 (bs, 1H), 10.07 (bs, 1H), 8.17 (d, J_{H-H} = 8.3 Hz, 1H), 8.12 (d, J_{H-H} = 8.2 Hz, 1H), 7.95 (d, J_{H-H} = 7.5 Hz, 2H), 7.68-7.56 (m, 5H), 7.28 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ: 146.7, 146.0, 142.3, 133.6 (CH), 129.5 (CH), 128.8 (CH), 127.8 (CH), 127.2 (CH), 126.7, 123.6 (CH), 122.8 (CH), 121.2, 104.2 (CH). HR MS (ESI) m/z: 301.0532 $[M + H]^+$ (calcd for $C_{16}H_{13}O_4S^+$ 301.0529).

*4.2.23. 4-Hydroxy-2,6-dimethyl-3-(phenylsulfonyl)phenyl benzenesulfonate (**4s**)*

Colorless solid, mp 107-108 °C. IR (KBr) ν(cm^{-1}): 3267, 1608, 1562, 1458, 1369, 1304, 1196, 1122, 1080. ^{1}H NMR (400 MHz, DMSO) δ: 10.84 (bs, 1H), 7.96 (d, J_{H-H} = 7.9 Hz, 2H), 7.88 (t, J_{H-H} = 7.4 Hz, 1H), 7.83 (d, J_{H-H} = 7.6 Hz, 2H), 7.72 (t, J_{H-H} = 7.8 Hz, 2H), 7.66 (d, J_{H-H} = 7.4 Hz, 1H), 7.58 (t, J_{H-H} = 7.8 Hz, 2H), 6.6 (s, 1H), 2.24 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 155.6, 143.3, 140.2, 139.9, 135.8, 135.6 (CH), 133.9, 133.5 (CH), 130.5 (CH), 129.3 (CH), 128.5 (CH), 127.3 (CH), 123.4, 117.9 (CH), 17.9 (CH_3), 14.9 (CH_3). HR MS (ESI) m/z: 419.0616 $[M + H]^+$ (calcd for $C_{20}H_{19}O_6S_2^+$ 419.0618).

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