

Article

TBAB-Catalyzed 1,6-Conjugate Sulfonylation of *para*-Quinone Methides: A Highly Efficient Approach to Unsymmetrical *gem*-Diarylmethyl Sulfones in Water [†]

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[†] Dedicated to Professor Jean-Marie Basset on the occasion of his 77th birthday.

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Abstract: A highly efficient sulfonylation of *para*-quinone methides with sulfonyl hydrazines in water has been developed on the basis of the mode involving a tetrabutyl ammonium bromide (TBAB)-promoted sulfa-1,6-conjugated addition pathway. This reaction provides a green and sustainable method to synthesize various unsymmetrical diarylmethyl sulfones, showing good functional group tolerance, scalability, and regioselectivity. Further transformation of the resulting diarylmethyl sulfones provides an efficient route to some functionalized molecules.

Keywords: sulfa-1,6-conjugated addition; unsymmetrical diarylmethyl sulfones; green and sustainable chemistry; synthesis in water

1. Introduction

As a class of sulfur-containing compounds, sulfones are widely used in organic synthesis, pharmaceuticals, agrochemicals, and materials science [1–7]. Among the sulfone family, diarylmethyl sulfones hold an essential position in biologically important compounds that show various biological activities, such as potassium channel inhibitory activity [8], as well as antidepressant [9] and anticancer properties (Figure 1) [10]. Additionally, diarylmethyl sulfones can be applied as useful intermediates for synthetic applications owing to the versatile reactivities of the sulfonyl group activated carbanions [1,11–14].

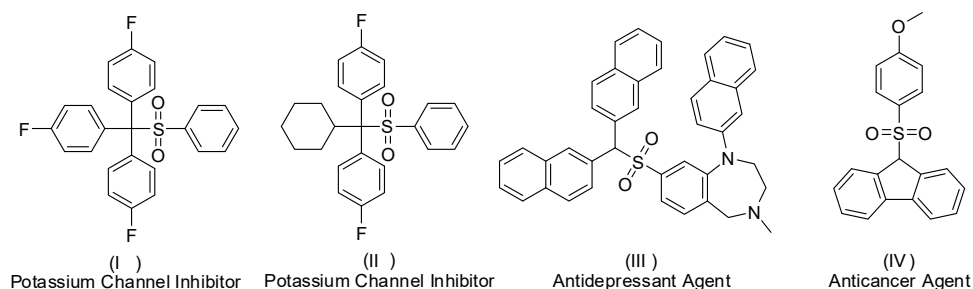


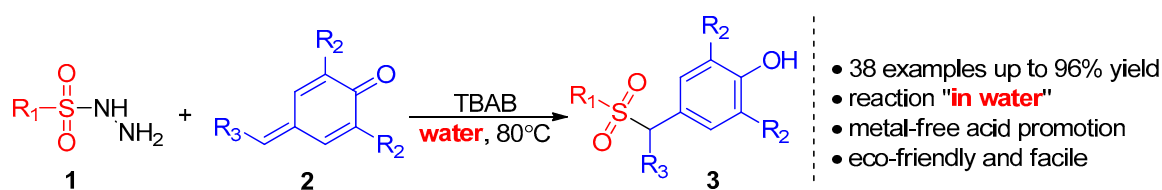
Figure 1. Representative biologically active diarylmethyl sulfone derivatives.

Although a number of methodologies have been developed for the synthesis of diarylmethyl sulfones, most of the reported methods suffer from the harsh reaction conditions, multi-step procedures,

and requirements of expensive metal catalysts or potentially toxic organic solvents [15–18], which make them unsustainable and environmentally unfavorable.

Concerns about the environmental issues caused by the influence of human society have currently become prevalent and ubiquitous. Engagement on green and sustainable methods of chemical synthesis has emerged as a pioneering realm [19–23] garnering of enormous attention of chemists and biologists. Among them, chemical reactions “in water” [24] offered a novel way to green and sustainable synthesis. Water, compared to the traditional organic solvents, possesses distinctive properties such as safety, innocuousness, high heat capacity, extensive hydrogen bonding, and redox stability [24–26]. Consequently, water has been gradually accepted [27–33] as a desirable reaction medium since the first water-promoted Diels–Alder reaction reported by Breslow [34] in 1980.

The C-S bond formation reaction is still an intriguing field attributed to the versatile block-building usages [35,36] and the bioactive agents [37,38] of sulfur-containing compounds. Thus, substantial endeavors have been focused on the achievement of the efficient, expedient, and low-cost approach. With our keen interest in the sulfa-1,6-conjugated addition reaction [15,39,40], we try to combine the green and sustainable chemical synthetic concept and the C-S bonding formation reactions. Herein, we disclose a highly efficient tetrabutyl ammonium bromide (TBAB)-promoted sulfonylation of *para*-quinone methide (*p*-QM) with sulfonyl hydrazines to afford unsymmetrical *gem*-diarylmethyl sulfones via a sulfa-1,6-conjugated addition pathway. All these reactions were performed smoothly in water under mild conditions (Scheme 1).



Scheme 1. Synthesis of unsymmetrical *gem*-diarylmethyl sulfones via sulfa-1,6-conjugated addition in water.

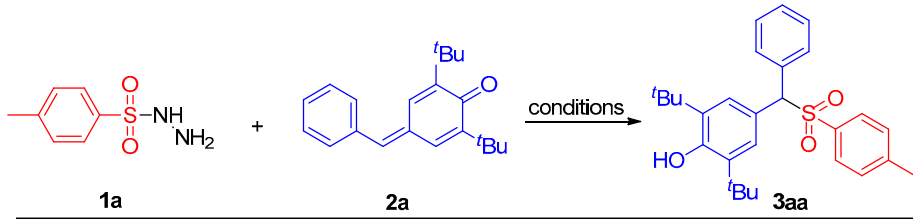
2. Results and Discussion

2.1. Optimization of Reaction Conditions

In our preliminary study, the investigation of the reaction conditions was carried out with 4-methylbenzenesulfonylhydrazide **1a** and *para*-quinone methides (*p*-QM) **2a** as model substrates (Table 1). Initially, the reaction was explored with different solvents in absence of a catalyst. When the reaction was carried out at 80 °C in tetrahydrofuran (THF), the desired 1,6-sulfa-conjugated adduct was obtained in mediate yield (50%). Other organic solvents including Et₂O, toluene, dichloroethane (DCE), dioxane, and dimethylsulfoxide (DMSO) were proved to be unsuitable for the reaction (Table 1, entry 1–6). It was found that protic polar solvent had an obvious promotion effect on the reaction. When H₂O and EtOH were employed, the yield was increased slightly to 61% and 73%, respectively (Table 1, entry 7–8). Although EtOH had a better effect than water, taking into consideration the “green and sustainable chemistry” perspective, we chose H₂O as a solvent. Subsequently, we focused on catalyst screening to improve the yield of the water mediated C-S bond formation reaction. Unfortunately, heterogeneous transition metal nano-catalysts such as Pd/C, Pd/TiO₂, Au/TiO₂, and Pt/C had little promotion effect on the reaction (Table 1, entry 9–12). Inspired by the better result of EtOH, phase transfer catalysts were selected to improve the solubility of organic substrate **1a** and **2a** in water, which may have a positive influence on the reaction (Table 1, entry 13–17). To our delight, in presence of 10% mol tetrabutylammonium bromide (TBAB), the yield was improved sharply to 82% (Table 1, entry 16). Based on the result, we continuously investigated the effect of other reaction parameters including temperature, reaction time, and reactant ratio. We were pleased to find that the yield was markedly increased, as the reactant ratio of **2a**:**1a** was increased from 1 to 1.5. Thus, the

desired *gem*-diarylmethyl sulfone **3aa** was obtained in 96% yield by performing the TBAB-catalyzed sulfonylation of 4-methylbenzenesulfonylhydrazide **1a** to *p*-QM **2a** at 80 °C in 12 h (Table 1, entry 22). Given either a lower or higher temperature, the yields decreased (Table 1, entry 18–20).

Table 1. Optimization of the reaction conditions for the 1,6-conjugate sulfonylation of 4-methylbenzenesulfonylhydrazide **1a** to *p*-QM **2a**^a.



Entry	Catalyst	Solvent	T (°C)	Time (h)	Yield ^b (%)
1	-	Et ₂ O	40	10	0
2	-	Toluene	80	10	0
3	-	THF	70	10	50
4	-	DCE	80	10	trace
5	-	Dioxane	80	10	trace
6	-	DMSO	80	10	trace
7	-	H ₂ O	80	10	61
8	-	EtOH	80	10	73
9	Pd/C	H ₂ O	80	10	75
10	Pd/TiO ₂	H ₂ O	80	10	53
11	Au/TiO ₂	H ₂ O	80	10	43
12	Pt/C	H ₂ O	80	10	70
13	CTAB	H ₂ O	80	10	51
14	TBAI	H ₂ O	80	10	78
15	TEBAC	H ₂ O	80	10	80
16	TBAB	H ₂ O	80	10	82
17	SDS	H ₂ O	80	10	18
18	TBAB	H ₂ O	90	10	81
19	TBAB	H ₂ O	60	10	63
20	TBAB	H ₂ O	30	10	15
21	TBAB	H ₂ O	80	12	90
22 ^c	TBAB	H ₂ O	80	12	96

^a The reaction conditions: **1a** (0.20 mmol), **2a** (0.20 mmol), catalyst (0.02 mmol), solvent (1 mL), ^b isolated yield based on **1a**, ^c **2a** (0.3 mmol).

2.2. Reaction Scope

Based on the optimized reaction conditions, the generality of this 1,6-conjugate sulfonylation reaction of sulfonyl hydrazines to *para*-quinone methides was investigated. Some of the results are summarized in Figures 2 and 3.

A number of *para*-quinone methide derivatives **2** bearing different substituents were explored with 4-methylbenzenesulfonylhydrazide **1a** under standard reaction condition (Figure 2). Various substituent groups, such as electron-donating groups (-Me, -OMe), electron-withdrawing groups (-CF₃, -NO₂), and halogen atoms (F, Cl, Br), on the *p*-QM derivatives' aryl ring at the *ortho* (**2ab–2ag**), *meta* (**2ah–2al**), and *para* (**2am–2as**) positions were well tolerated by the reaction to provide the corresponding sulfonylation adducts in good to excellent yields. Furthermore, non-substituted phenyl substrate **2aa**, disubstituted 2,4-dichlorophenyl substrate **2at**, polycyclic aromatic substrate **2av**, heteroaromatic substrates **2au**, and aliphatic substrate **2ay** led to the desired product in 63–95% yields, implying the well-tolerated property of the substrates in this reaction. Moreover, *p*-QMs derived from 2,6-dimethylphenol **2aw** and 2,6-diisopropylphenol **2ax** were also compatible to afford the

corresponding adducts, while the former was in lower yield (**3aw**, 63%) probably due to its small steric hindrance around the phenolic hydroxyl group.

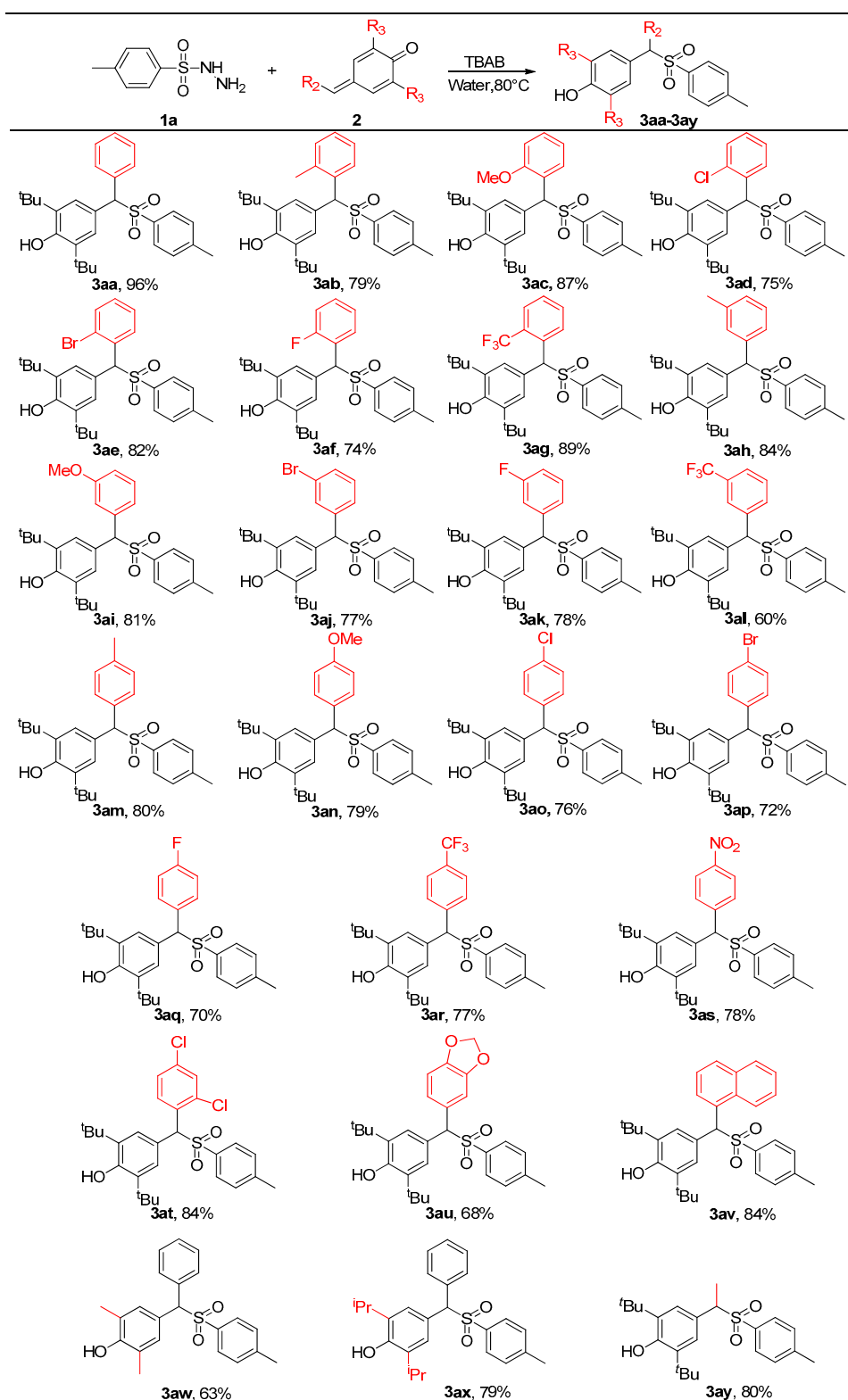


Figure 2. Tetrabutylammonium bromide (TBAB)-catalyzed 1,6-conjugate sulfonylation for synthesis of *gem*-diarylmethyl sulfones **3aa–3ay**. ^a The reaction conditions: sulfonamide **1a** (0.20 mmol), *p*-QM **2** (0.30 mmol), TBAB (0.02 mmol) in 1 mL of H₂O, 80 °C, 12 h, ^b Isolated yield base on **1a**.

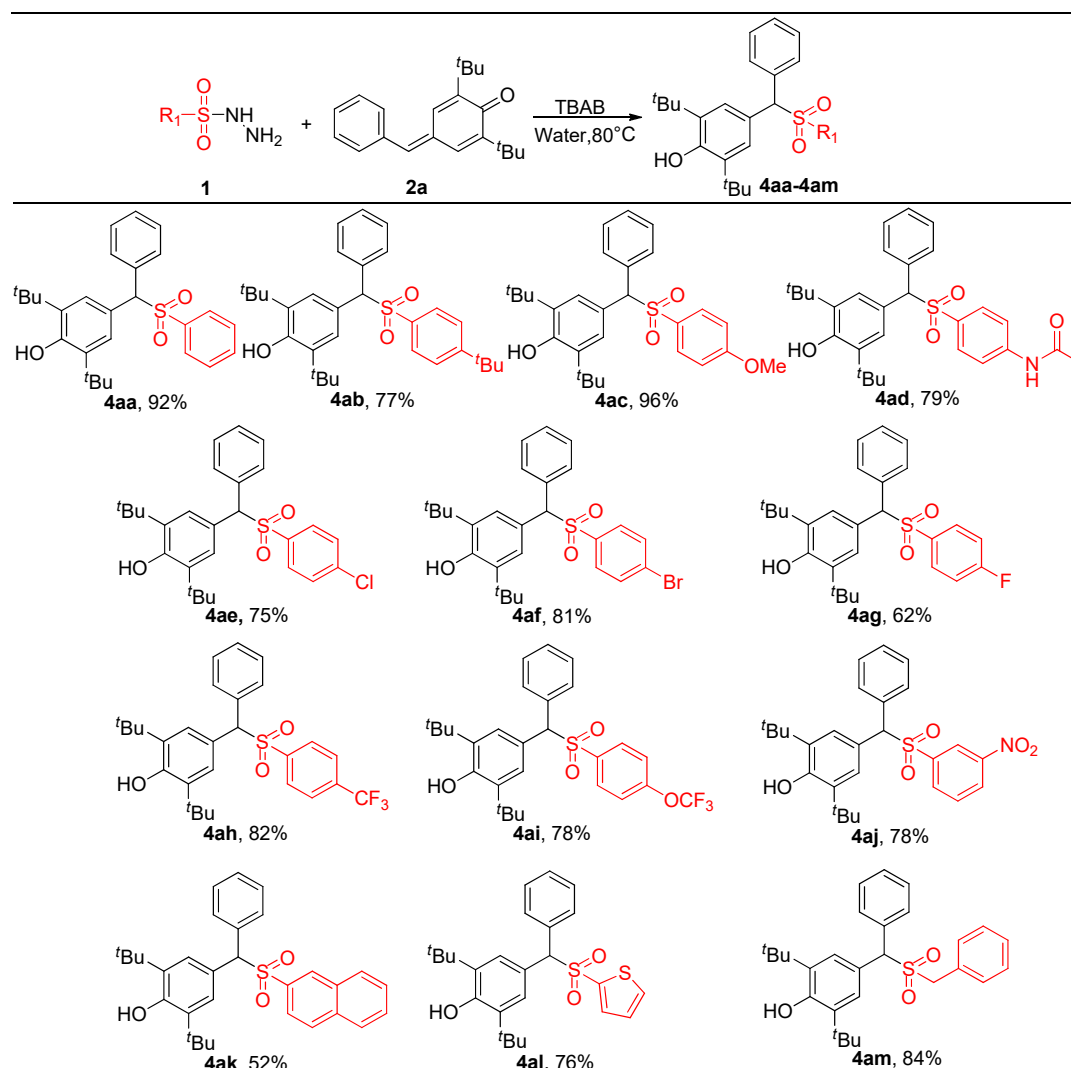


Figure 3. TBAB catalyzed 1,6-conjugate sulfonylation for synthesis of *gem*-diarylmethyl sulfones 4aa–4am. ^a The reaction conditions: sulfonyl hydrazides **1** (0.20 mmol), *para*-quinone methide (*p*-QM) **2a** (0.30 mmol), TBAB (0.02 mmol) in 1 mL of H₂O, 80 °C, 12h, ^b isolated yield base on **1**.

Consequently, we investigated the substitute effects of sulfonyl hydrazines by using 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone **2a** as model substrate under optimized reaction condition (Figure 3). In general, a wide range of sulfonyl hydrazines **1** bearing *meta* and *para* substituent group including electron-donating groups (-Me, -OMe, -NHAc, -OCF₃), electron-withdrawing groups (-CF₃, -NO₂), and halogen atom (F, Cl, Br) reacted smoothly with *p*-QM **2a**, affording the adducts in 62–96% yields. In addition, phenyl **4aa**, *p*-*tert*-butyl phenyl **4ab**, 2-naphthyl **4ak**, thienyl **4al** and aliphatic benzyl substituted sulfonyl hydrazines were also tolerated by the reaction to produce the final products in 52–92% yields.

2.3. Proposed Mechanism

The chemical structure of diarylmethyl sulfones **3** and **4** were characterized by nuclear magnetic resonance spectroscopies (Supplementary Materials). Because there is another possible sulfinic ester adduct, the two potential products cannot be distinguished by NMR. To further identify the structure of the products, **4af** was selected as a representative compound, and the sulfone structure was unequivocally confirmed by single crystal X-ray diffraction analysis, as shown in Figure 4 (CCDC No. 1531154).

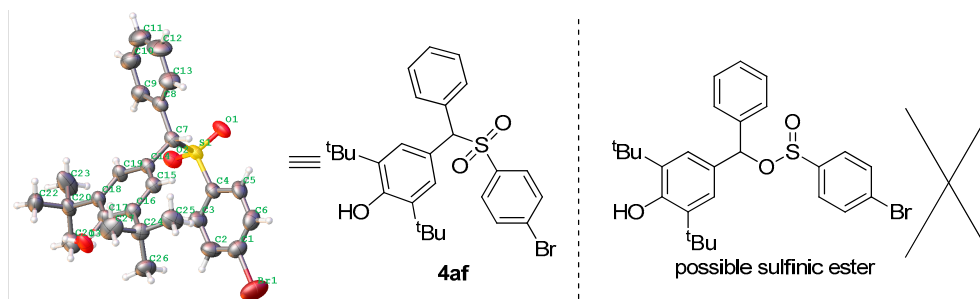
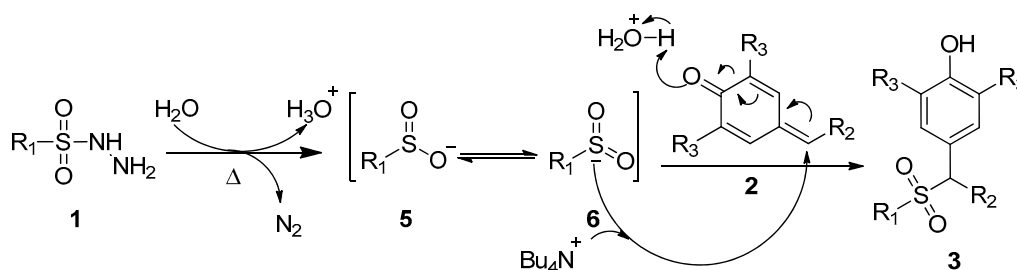


Figure 4. Crystal structure of diarylmethyl sulfone **4af** and possible sulfinic ester.

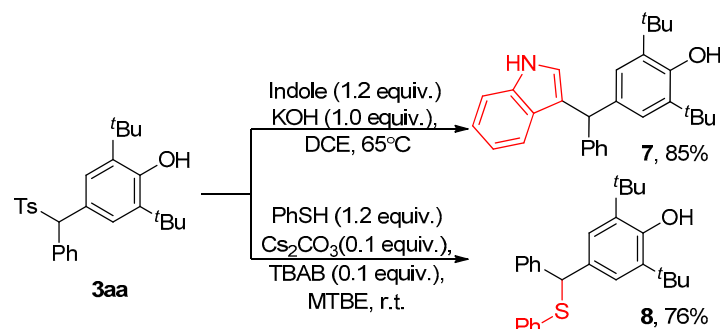
On the basis of the above observations, we tentatively propose a plausible reaction mechanism (Scheme 2). First, the sulfonyl hydrazines **1** decomposed into sulfinyl anion **5** with the N_2 released and hydronium generation under the heating condition. Intermediate **5** has a resonate equilibrium with sulfur-centered anion **6** in water. As a more reactive species, the sulfur-centered anion **6** attacks the electrophilic atom of the resonated structure of *p*-QM **2** with the help of tetrabutylammonium bromide (TBAB). Finally, driven by the aromatization force, the target product is obtained.



Scheme 2. Probable mechanism of the sulfa-1,6-conjugate reactions in water.

2.4. Derivatives of Products

To further demonstrate the synthetic utility of this protocol, the transformations of products were then explored (Scheme 3). A carbon-carbon bond formation between **3aa** and indole led to the generation of unsymmetrical triarylmethane **7**. Furthermore, base-promoted carbon-sulfur bond formation between **3aa** and thiophenol proceeded to the facial delivery of unsymmetrical *gem*-diarylmethyl thioether **8**. Moreover, the yield of products of both synthesis routines reached around 80%, implying the potential and feasibility of further application of **3aa**.



Scheme 3. Synthetic utility of diarylmethyl sulfone **3aa**.

3. Materials and Methods

3.1. General Information

$^1\text{H-NMR}$, $^{13}\text{C-NMR}$ spectra were obtained utilizing a Bruker 600 and 400 MHz instrument and reported in CDCl_3 or $\text{DMSO}(d_6)$. ^1H and $^{13}\text{C-NMR}$ chemical shifts are reported in ppm relative to either TMS (^1H) ($\delta = 0$ ppm) as an internal standard or the residual solvent peak as following: $\text{CDCl}_3 = 7.26$ ($^1\text{H-NMR}$), $(\text{CD}_3)_2\text{SO} = 2.50$ ($^1\text{H-NMR}$), $\text{CDCl}_3 = 77.16$ ($^{13}\text{C-NMR}$), $(\text{CD}_3)_2\text{SO} = 40.00$ ($^{13}\text{C-NMR}$). HRMS were performed on a Bruker Impact II 10200 instrument. Commercially available chemicals and solvents were purchased from Adamas-beta, Energy Chemical, Chongqing Chuandong Chemical, and Chengdu Kelong Chemical. The corresponding compounds were synthesized according to the methods reported in the literature. Analytical thin-layer chromatography (TLC) was performed on silicycle silica gel plates with F-254 indicator, and compounds were visualized by irradiation with UV light. Chromatography was carried out using silica gel 300–400 mesh.

3.2. Experiment

3.2.1. Representative Procedure for Synthesis of Gem-Diarylmethyl Sulfones

To a solution of corresponding 4-(arylmethylidene)-2,6-di-*tert*-butylcyclohexa-2,5-dienone (0.3 mmol) in 1 mL water, the corresponding arylsulfonohydrazide (0.2 mmol) and TBAB (0.02 mmol) were added. The mixture was stirred at 80°C . The reaction was monitored by TLC. After complete reaction, the mixture was extracted by ethyl acetate, dried over by anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was then purified by flash column chromatography on silica gel (gradient eluent of PE/EA = 30:1–10:1) to gain the corresponding product.

2,6-Di-tert-butyl-4-(phenyl(tosyl)methyl)phenol (3aa): [15] Pale yellow solid; 96% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.61 (d, $J = 7.1$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.32 (dq, $J = 14.2, 6.9$ Hz, 3H), 7.16 (s, 2H), 7.13 (d, $J = 7.9$ Hz, 2H), 5.20 (s, 1H), 5.16 (s, 1H), 2.36 (s, 3H), 1.35 (s, 18H); $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 154.08 (s), 144.00 (s), 135.94 (s), 135.77 (s), 133.66 (s), 130.00 (s), 129.10 (s), 129.05 (s), 128.62 (s), 128.36 (s), 127.10 (s), 123.57 (s), 76.90 (s), 34.31 (s), 30.16 (s), 21.48 (s).

2,6-Di-tert-butyl-4-(o-tolyl(tosyl)methyl)phenol (3ab): [15] Pale yellow solid; 76% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 8.23 (d, $J = 7.8$ Hz, 1H), 7.44 (d, $J = 8.0$ Hz, 2H), 7.30 (t, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 7.4$ Hz, 1H), 7.14 (d, $J = 8.0$ Hz, 2H), 7.13 (s, 2H), 7.08 (d, $J = 7.5$ Hz, 1H), 5.43 (s, 1H), 5.21 (s, 1H), 2.37 (s, 3H), 2.17 (s, 3H), 1.34 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 153.99 (s), 143.87 (s), 138.20 (s), 135.84 (s), 130.49 (s), 129.84 (s), 129.33 (s), 129.09 (s), 128.99 (s), 127.03 (s), 123.75 (s), 76.67 (s), 34.28 (s), 30.13 (s), 21.47 (s), 21.09 (s).

2,6-Di-tert-butyl-4-((2-methoxyphenyl)(tosyl)methyl)phenol (3ac): [15] Pale yellow solid; 87% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 8.14 (d, $J = 7.6$ Hz, 1H), 7.44 (d, $J = 7.9$ Hz, 2H), 7.22–7.25 (m, 3H), 7.13 (d, $J = 7.8$ Hz, 2H), 7.04 (t, $J = 7.5$ Hz, 1H), 6.73 (d, $J = 8.2$ Hz, 1H), 5.93 (s, 1H), 5.19 (s, 1H), 3.60 (s, 3H), 2.36 (s, 3H), 1.36 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz) δ 156.98 (s), 153.95 (s), 143.67 (s), 136.30 (s), 135.69 (s), 129.86 (s), 129.39 (s), 129.08 (s), 128.82 (s), 127.36 (s), 123.53 (s), 122.54 (s), 120.69 (s), 110.79 (s), 66.98 (s), 55.56 (s), 34.30 (s), 30.17 (s), 21.46 (s).

2,6-Di-tert-butyl-4-((2-chlorophenyl)(tosyl)methyl)phenol (3ad): [15] Pale yellow solid; 75% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 8.35 (d, $J = 7.9$ Hz, 1H), 7.46 (d, $J = 8.1$ Hz, 2H), 7.37 (t, $J = 7.6$ Hz, 1H), 7.29 (d, $J = 8.0$ Hz, 1H), 7.23 (t, $J = 7.7$ Hz, 1H), 7.16 (s, 3H), 7.15 (s, 1H), 5.88 (s, 1H), 5.23 (s, 1H), 2.37 (s, 3H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 153.20 (s), 143.25 (s), 134.90 (s), 134.72 (s), 133.87 (s), 131.18 (s), 129.10 (s), 128.80 (s), 128.38 (s), 128.17 (s), 128.01 (s), 126.25 (s), 126.05 (s), 121.54 (s), 70.08 (s), 33.28 (s), 29.11 (s), 20.52 (s).

4-((2-Bromophenyl)(tosyl)methyl)-2,6-di-tert-butylphenol (3ae): [15] Pale yellow solid; 82% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 8.35 (d, $J = 7.8$ Hz, 1H), 7.47 (d, $J = 7.9$ Hz, 3H), 7.41 (t, $J = 7.6$ Hz, 1H), 7.18 (s,

2H), 7.15 (m, 3H), 5.90 (s, 1H), 5.23 (s, 1H), 2.37 (s, 3H), 1.36 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 154.19 (s), 144.25 (s), 135.92 (s), 135.77 (s), 133.88 (s), 133.17 (s), 130.19 (s), 129.64 (s), 129.18 (s), 129.01 (s), 127.69 (s), 127.24 (s), 126.02 (s), 122.56 (s), 73.83 (s), 34.29 (s), 30.13 (s), 21.51 (s).

2,6-Di-tert-butyl-4-((2-fluorophenyl)(tosyl)methyl)phenol (3af): [15] Pale yellow solid; 74% yield. ^1H -NMR (600 MHz, CDCl_3) δ 8.21 (t, $J = 7.2$ Hz, 1H), 7.46 (d, $J = 8.0$ Hz, 2H), 7.29 (dd, $J = 13.2, 6.3$ Hz, 1H), 7.27–7.22 (m, 1H), 7.16 (s, 3H), 7.15 (s, 1H), 6.96 (t, $J = 9.1$ Hz, 1H), 5.63 (s, 1H), 5.24 (s, 1H), 2.37 (s, 3H), 1.35 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 160.61 (d, $J_{\text{C-F}} = 247.4$ Hz), 154.22 (s), 144.23 (s), 135.96 (s), 135.57 (s), 130.15 (d, $J_{\text{C-F}} = 1.6$ Hz), 129.97 (d, $J_{\text{C-F}} = 8.6$ Hz), 129.14 (s), 129.05 (s), 127.19 (s), 124.30 (d, $J_{\text{C-F}} = 3.6$ Hz), 122.73 (s), 121.57 (d, $J_{\text{C-F}} = 13.5$ Hz), 115.50 (d, $J_{\text{C-F}} = 23.0$ Hz), 67.18 (d, $J_{\text{C-F}} = 4.2$ Hz), 34.29 (s), 30.10 (s), 21.50 (s).

2,6-Di-tert-butyl-4-(tosyl(2-(trifluoromethyl)phenyl)methyl)phenol (3ag): [15] Pale yellow solid; 89% yield. ^1H -NMR (600 MHz, CDCl_3) δ 8.61 (d, $J = 7.9$ Hz, 1H), 7.68 (t, $J = 7.7$ Hz, 1H), 7.62 (d, $J = 7.8$ Hz, 1H), 7.44 (m, 3H), 7.15 (m, 4H), 5.59 (s, 1H), 5.23 (s, 1H), 2.36 (s, 3H), 1.34 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 154.20 (s), 144.34 (s), 135.87 (s), 135.59 (s), 133.00 (s), 131.99 (s), 130.47 (s), 129.18 (s), 129.10 (s), δ 129.64–128.96 (m), 128.25 (s), 127.10 (s), 126.45 (q, $J_{\text{C-F}} = 5.9$ Hz), 124.12 (q, $J_{\text{C-F}} = 274.4$ Hz), 122.73 (s), 71.00 (s), 34.29 (s), 30.10 (s), 21.48 (s).

2,6-Di-tert-butyl-4-(m-tolyl(tosyl)methyl)phenol (3ah): [15] Pale yellow solid; 84% yield. ^1H -NMR (600 MHz, CDCl_3) δ 7.46 (d, $J = 7.5$ Hz, 1H), 7.42 (d, $J = 7.7$ Hz, 2H), 7.39 (s, 1H), 7.28–7.19 (m, 1H), 7.13 (m, 5H), 5.20 (s, 1H), 5.12 (s, 1H), 2.35 (d, $J = 9.0$ Hz, 3H), 2.33 (s, 3H), 1.35 (s, 18H); ^{13}C -NMR (151 MHz, CDCl_3) δ 154.03 (s), 143.92 (s), 138.21 (s), 135.84 (s), 135.81 (s), 133.43 (s), 130.86 (s), 129.12 (s), 128.99 (s), 128.49 (s), 127.10 (s), 126.88 (s), 123.65 (s), 76.92 (s), 34.28 (s), 30.12 (s), 21.46 (s).

2,6-Di-tert-butyl-4-((3-methoxyphenyl)(tosyl)methyl)phenol (3ai): [15] Pale yellow solid; 81% yield. ^1H -NMR (600 MHz, CDCl_3) δ 7.43 (d, $J = 7.8$ Hz, 2H), 7.27–7.23 (m, 1H), 7.19 (d, $J = 5.4$ Hz, 2H), 7.17–7.11 (m, 4H), 6.86 (d, $J = 8.0$ Hz, 1H), 5.21 (s, 1H), 5.13 (s, 1H), 3.79 (s, 3H), 2.36 (s, 3H), 1.35 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 159.65 (s), 154.08 (s), 143.99 (s), 135.87 (s), 135.74 (s), 134.93 (s), 129.53 (s), 129.11 (s), 129.03 (s), 127.07 (s), 123.45 (s), 122.39 (s), 115.33 (s), 114.42 (s), 76.78 (s), 55.22 (s), 34.29 (s), 30.13 (s), 21.47 (s).

4-((3-Bromophenyl)(tosyl)methyl)-2,6-di-tert-butylphenol (3aj): [15] Pale yellow solid; 77% yield. ^1H -NMR (600 MHz, CDCl_3) δ 7.69 (s, 1H), 7.66 (d, $J = 7.8$ Hz, 1H), 7.45 (d, $J = 8.0$ Hz, 1H), 7.42 (d, $J = 8.1$ Hz, 2H), 7.23 (t, $J = 7.9$ Hz, 1H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.10 (s, 2H), 5.24 (s, 1H), 5.11 (s, 1H), 2.37 (s, 3H), 1.35 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 154.24 (s), 144.32 (s), 136.08 (s), 135.82 (s), 135.35 (s), 133.15 (s), 131.46 (s), 130.07 (s), 129.16 (s), 129.10 (s), 128.34 (s), 127.02 (s), 122.90 (s), 122.55 (s), 76.15 (s), 34.31 (s), 30.10 (s), 21.49 (s).

2,6-Di-tert-butyl-4-((3-fluorophenyl)(tosyl)methyl)phenol (3ak): [15] Pale yellow solid; 78% yield. ^1H -NMR (400 MHz, CDCl_3) δ 7.43 (d, $J = 8.2$ Hz, 2H), 7.41–7.36 (m, 2H), 7.31 (td, $J = 8.0, 6.0$ Hz, 1H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.11 (s, 2H), 7.02 (tdd, $J = 8.4, 2.5, 0.8$ Hz, 1H), 5.25 (s, 1H), 5.15 (s, 1H), 2.37 (s, 3H), 1.35 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 162.67 (d, $J_{\text{C-F}} = 246.5$ Hz), 154.23 (s), 144.24 (s), 136.06 (s), 135.91 (d, $J_{\text{C-F}} = 7.3$ Hz), 135.46 (s), 130.02 (d, $J_{\text{C-F}} = 8.3$ Hz), 129.13 (s), 129.08 (s), 127.01 (s), 125.71 (d, $J_{\text{C-F}} = 2.8$ Hz), 123.04 (s), 117.05 (d, $J_{\text{C-F}} = 23.0$ Hz), 115.35 (d, $J_{\text{C-F}} = 21.1$ Hz), 76.22 (s), 34.29 (s), 30.10 (s), 21.43 (s).

2,6-Di-tert-butyl-4-(tosyl(3-(trifluoromethyl)phenyl)methyl)phenol (3al): [15] Pale yellow solid; 60% yield. ^1H -NMR (600 MHz, CDCl_3) δ 7.91 (d, $J = 7.7$ Hz, 1H), 7.81 (s, 1H), 7.58 (d, $J = 7.7$ Hz, 1H), 7.49 (t, $J = 7.8$ Hz, 1H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.15 (s, 1H), 7.13 (s, 3H), 5.27 (s, 1H), 5.23 (s, 1H), 2.36 (s, 3H), 1.35 (s, 18H). ^{13}C -NMR (151 MHz, CDCl_3) δ 154.33 (s), 144.47 (s), 136.20 (s), 135.18 (s), 134.71 (s), 133.22 (s), 130.94 (q, $J_{\text{C-F}} = 32.5$ Hz), 129.20 (s), 129.11 (d, $J_{\text{C-F}} = 3.5$ Hz), 127.20–126.83 (m), 125.29–125.02 (m), 123.90 (q, $J_{\text{C-F}} = 272.4$ Hz), 122.70 (s), 76.29 (s), 34.32 (s), 30.08 (s), 21.45 (s).

2,6-Di-tert-butyl-4-(p-tolyl(tosyl)methyl)phenol (3am): [15] Pale yellow solid; 80% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.50 (d, $J = 8.0$ Hz, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 7.15 (d, $J = 8.2$ Hz, 4H), 7.12 (d, $J = 8.1$ Hz, 2H), 5.19 (s, 1H), 5.13 (s, 1H), 2.36 (s, 3H), 2.33 (s, 3H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 153.99 (s), 143.87 (s), 138.20 (s), 135.84 (s), 130.49 (s), 129.84 (s), 129.33 (s), 129.09 (s), 128.99 (s), 127.03 (s), 123.75 (s), 76.67 (s), 34.28 (s), 30.13 (s), 21.47 (s), 21.09 (s).

2,6-Di-tert-butyl-4-((4-methoxyphenyl)(tosyl)methyl)phenol (3an): [15] Pale yellow solid; 79% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.53 (d, $J = 8.6$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.15 (s, 2H), 7.12 (d, $J = 8.0$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 5.20 (s, 1H), 5.13 (s, 1H), 3.79 (s, 3H), 2.35 (s, 3H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 155.77 (s), 150.04 (s), 139.94 (s), 131.93 (s), 131.87 (s), 127.28 (s), 125.13 (s), 125.08 (s), 123.06 (s), 121.53 (s), 119.87 (s), 110.15 (s), 72.34 (s), 51.33 (s), 30.35 (s), 27.78–23.72 (m), 17.53 (s).

2,6-Di-tert-butyl-4-((4-chlorophenyl)(tosyl)methyl)phenol (3ao): [15] Pale yellow solid; 81% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.57 (d, $J = 8.4$ Hz, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.4$ Hz, 2H), 7.14 (d, $J = 8.1$ Hz, 2H), 7.09 (s, 2H), 5.23 (s, 1H), 5.14 (s, 1H), 2.37 (s, 3H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 154.18 (s), 144.23 (s), 136.05 (s), 135.45 (s), 134.54 (s), 132.16 (s), 131.25 (s), 129.15 (s), 129.07 (s), 128.82 (s), 126.96 (s), 123.10 (s), 76.05 (s), 34.30 (s), 30.10 (s), 21.50 (s).

4-((4-Bromophenyl)(tosyl)methyl)-2,6-di-tert-butylphenol (3ap): [15] Pale yellow solid; 79% yield. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 7.54–7.45 (m, 4H), 7.42 (d, $J = 8.2$ Hz, 2H), 7.15 (d, $J = 8.1$ Hz, 2H), 7.09 (s, 2H), 5.24 (s, 1H), 5.13 (s, 1H), 2.37 (s, 3H), 1.34 (s, 18H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 154.20 (s), 144.28 (s), 136.02 (s), 135.35 (s), 132.67 (s), 131.79 (s), 131.54 (s), 129.17 (s), 129.06 (s), 126.95 (s), 122.98 (s), 122.76 (s), 76.08 (s), 34.30 (s), 30.10 (s), 21.53 (s).

2,6-Di-tert-butyl-4-((4-fluorophenyl)(tosyl)methyl)phenol (3aq): [15] Pale yellow solid; 70% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.60 (dd, $J = 8.2, 5.4$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H), 7.14 (d, $J = 8.0$ Hz, 2H), 7.12 (s, 2H), 7.04 (t, $J = 8.5$ Hz, 2H), 5.23 (s, 1H), 5.16 (s, 1H), 2.36 (s, 3H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 162.79 (d, $J_{\text{C-F}} = 248.1$ Hz), 154.13 (s), 144.15 (s), 136.03 (s), 135.54 (s), 131.73 (d, $J_{\text{C-F}} = 8.2$ Hz), 129.44 (d, $J_{\text{C-F}} = 3.2$ Hz), 129.11 (s), 129.06 (s), 126.97 (s), 123.33 (s), 115.57 (d, $J_{\text{C-F}} = 21.5$ Hz), 75.98 (s), 34.30 (s), 30.11 (s), 21.47 (s).

2,6-Di-tert-butyl-4-(tosyl(4-(trifluoromethyl)phenyl)methyl)phenol (3ar): [15] Pale yellow solid; 77% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.78 (d, $J = 8.1$ Hz, 2H), 7.62 (d, $J = 8.2$ Hz, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.09 (s, 2H), 5.25 (s, 1H), 5.22 (s, 1H), 2.37 (s, 3H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 154.29 (s), 144.41 (s), 137.69 (s), 136.17 (s), 135.29 (s), 130.55 (q, $J_{\text{C-F}} = 32.6$ Hz), 130.28 (s), 129.18 (s), 129.07 (s), 126.97 (s), 125.53 (q, $J_{\text{C-F}} = 3.6$ Hz), 123.96 (q, $J_{\text{C-F}} = 272.1$ Hz), 122.83 (s), 76.32 (s), 34.30 (s), 30.08 (s), 21.49 (s).

2,6-Di-tert-butyl-4-((4-nitrophenyl)(tosyl)methyl)phenol (3as): [15] Pale yellow solid; 72% yield. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.22 (d, $J = 8.9$ Hz, 2H), 7.85 (d, $J = 8.8$ Hz, 2H), 7.43 (d, $J = 8.3$ Hz, 2H), 7.17 (d, $J = 8.0$ Hz, 2H), 7.07 (s, 2H), 5.29 (s, 1H), 5.27 (s, 1H), 2.38 (s, 3H), 1.34 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 153.76 (s), 148.51 (d, $J = 2.9$ Hz), 147.13 (s), 143.63 (s), 137.22 (s), 136.63 (s), 129.98 (s), 129.55 (s), 128.21 (s), 127.26 (s), 124.18 (s), 123.50 (s), 61.32 (s), 34.31 (s), 30.04 (s), 21.45 (s).

2,6-Di-tert-butyl-4-((2,4-dichlorophenyl)(tosyl)methyl)phenol (3at): [15] Pale yellow solid; 68% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 8.29 (d, $J = 8.5$ Hz, 1H), 7.46 (d, $J = 8.0$ Hz, 2H), 7.37 (d, $J = 8.5$ Hz, 1H), 7.33 (s, 1H), 7.18 (d, $J = 7.9$ Hz, 2H), 7.10 (s, 2H), 5.79 (s, 1H), 5.25 (s, 1H), 2.39 (s, 1H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 154.31 (s), 144.50 (s), 136.06 (s), 135.56 (s), 135.47 (s), 134.79 (s), 130.90 (s), 130.83 (s), 129.62 (s), 129.29 (s), 128.99 (s), 127.44 (s), 127.08 (s), 122.18 (s), 70.63 (s), 34.29 (s), 30.09 (s), 21.53 (s).

2,6-Di-tert-butyl-4-((1,3-dihydroisobenzofuran-4-yl)(tosyl)methyl)phenol (3au): [15] Pale yellow solid; 68% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.43 (d, $J = 8.1$ Hz, 1H), 7.20 (s, 1H), 7.13 (d, $J = 9.6$ Hz, 1H), 7.01 (d, $J = 8.1$ Hz, 1H), 6.76 (d, $J = 8.1$ Hz, 1H), 5.95 (d, $J = 3.4$ Hz, 1H), 5.21 (s, 1H), 5.08 (s, 1H), 2.36 (s,

1H), 1.35 (s, 1H). ¹³C-NMR (151 MHz, CDCl₃) δ 154.19 (s), 148.02 (s), 147.93 (s), 144.14 (s), 136.09 (s), 135.86 (s), 129.20 (s), 127.14 (s), 127.03 (s), 124.14 (s), 123.83 (s), 110.36 (s), 108.45 (s), 101.37 (s), 76.60 (s), 34.43 (s), 32.20–27.96 (m), 21.62 (s); HRMS calculated for [M + Na]⁺ C₂₉H₃₄O₅SNa⁺, m/z 517.2019, found 517.2020.

2,6-Di-tert-butyl-4-(naphthalen-1-yl(tosyl)methyl)phenol (3av): [15] Pale yellow solid; 78% yield. ¹H-NMR (600 MHz, CDCl₃) δ 8.55 (d, *J* = 7.2 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.82 (t, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.45–7.39 (m, 2H), 7.25 (s, 1H), 7.14 (s, 1H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.05 (s, 1H), 5.19 (s, 1H), 2.33 (s, 3H), 1.31 (s, 18H). ¹³C-NMR (151 MHz, CDCl₃) δ 154.12 (s), 144.09 (s), 136.00 (s), 135.77 (s), 134.12 (s), 131.79 (s), 129.79 (s), 129.16 (s), 129.13 (s), 128.92 (s), 127.32 (s), 126.85 (s), 126.50 (s), 125.49 (s), 125.32 (s), 123.36 (s), 122.37 (s), 71.18 (s), 34.24 (s), 30.08 (s), 21.46 (s).

2,6-Dimethyl-4-(phenyl(tosyl)methyl)phenol (3aw): [15] Pale yellow solid; 63% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.54–7.44 (m, 4H), 7.28 (m, 3H), 7.15 (m, 4H), 5.13 (s, 1H), 4.70 (s, 1H), 2.37 (s, 3H), 2.20 (s, 6H). ¹³C-NMR (151 MHz, CDCl₃) δ 152.62 (s), 144.22 (s), 135.65 (s), 133.77 (s), 130.25 (s), 129.86 (s), 129.15 (s), 129.08 (s), 128.56 (s), 128.35 (s), 124.34 (s), 123.28 (s), 76.09 (s), 21.53 (s), 15.90 (s).

2,6-Diisopropyl-4-(phenyl(tosyl)methyl)phenol (3ax): [15] Pale yellow solid; 79% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.59 (d, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.37–7.28 (m, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 7.09 (s, 1H), 5.20 (s, 1H), 4.81 (s, 1H), 3.19–2.90 (m, 1H), 2.35 (s, 1H), 1.22 (d, *J* = 6.9 Hz, 1H), 1.14 (d, *J* = 6.8 Hz, 1H). ¹³C-NMR (151 MHz, CDCl₃) δ 150.23 (s), 144.02 (s), 133.77 (s), 133.48 (s), 129.99 (s), 129.08 (s), 129.05 (s), 128.58 (s), 128.36 (s), 125.59 (s), 124.87 (s), 99.99 (s), 76.62 (s), 27.21 (s), 22.61 (s), 22.53 (s), 21.48 (s).

2,6-Di-tert-butyl-4-(1-tosylethyl)phenol (3ay): [15] Pale yellow solid; 80% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.33 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.78 (s, 2H), 5.21 (s, 1H), 4.13 (q, *J* = 7.2 Hz, 1H), 2.38 (s, 3H), 1.77 (d, *J* = 7.2 Hz, 3H), 1.32 (s, 18H). ¹³C-NMR (151 MHz, CDCl₃) δ 154.13 (s), 143.98 (s), 135.75 (s), 134.32 (s), 129.31 (s), 129.04 (s), 126.21 (s), 124.39 (s), 66.53 (s), 34.23 (s), 30.13 (s), 21.50 (s), 13.45 (s).

2,6-Di-tert-butyl-4-(phenyl(phenylsulfonyl)methyl)phenol (4aa): [16] Pale yellow solid; 92% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.62 (d, *J* = 7.2 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.34 (dd, *J* = 15.7, 8.5 Hz, 5H), 7.19 (s, 2H), 5.24 (s, 1H), 5.21 (s, 1H), 1.36 (s, 18H). ¹³C-NMR (151 MHz, CDCl₃) δ 154.15 (s), 138.65 (s), 135.97 (s), 133.45 (s), 133.13 (s), 130.00 (s), 129.08 (s), 128.67 (s), 128.47 (s), 128.44 (s), 127.10 (s), 123.29 (s), 34.34 (s), 30.18 (s).

2,6-Di-tert-butyl-4-(((4-tert-butyl)phenyl)sulfonyl)(phenyl)methyl)phenol (4ab): [16] Pale yellow solid; 77% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.63 (d, *J* = 7.1 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.38–7.30 (m, 5H), 7.12 (s, 2H), 5.21 (s, 1H), 5.18 (s, 1H), 1.34 (s, 18H), 1.29 (s, 9H). ¹³C-NMR (151 MHz, CDCl₃) δ 157.07 (s), 154.04 (s), 135.85 (s), 135.59 (s), 133.66 (s), 129.96 (s), 129.01 (s), 128.60 (s), 128.33 (s), 127.13 (s), 125.42 (s), 123.57 (s), 76.88 (s), 35.12 (s), 34.29 (s), 31.04 (s), 30.16 (s).

2,6-Di-tert-butyl-4-(((4-methoxyphenyl)sulfonyl)(phenyl)methyl)phenol (4ac): [16] Pale yellow solid; 96% yield. ¹H-NMR (400 MHz, CDCl₃) δ 7.61 (d, *J* = 7.3 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.39–7.28 (m, 3H), 7.18 (s, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.23 (s, 1H), 5.16 (s, 1H), 3.81 (s, 3H), 1.36 (s, 18H). ¹³C-NMR (101 MHz, CDCl₃) δ 154.29 (s), 137.65 (s), 136.11 (s), 133.01 (s), 131.68 (s), 130.54 (s), 129.95 (s), 128.78 (s), 128.65 (s), 128.53 (s), 127.08 (s), 122.89 (s), 76.97 (s), 34.32 (s), 30.13 (s).

N-(4-(((3,5-di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)sulfonyl)phenyl)acetamide (4ad): Pale yellow solid; 79% yield. ¹H-NMR (600 MHz, DMSO-d₆) δ 10.28 (s, 1H), 7.61 (dd, *J* = 11.6, 8.3 Hz, 4H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.30 (t, *J* = 7.2 Hz, 1H), 7.23 (s, 2H), 7.03 (s, 1H), 5.77 (s, 1H), 2.06 (s, 3H), 1.31 (s, 18H). ¹³C-NMR (151 MHz, DMSO-d₆) δ 169.47 (s), 154.32 (s), 144.13 (s), 139.25 (s), 134.72 (s), 130.26 (s), 130.14 (s), 128.86 (s), 128.55 (s), 126.96 (s), 124.72 (s), 118.24 (s), 74.46 (s), 34.96 (s), 30.68 (s), 24.62 (s); HRMS (ESI): *m/z* calcd for C₂₉H₃₅NO₄SNa [M + Na]⁺, 516.2178; found, 516.2179.

2,6-Di-tert-butyl-4-(((4-chlorophenyl)sulfonyl)(phenyl)methyl)phenol (4ae): [16] Pale yellow solid; 75% yield. $^1\text{H-NMR}$ (600 MHz, DMSO(d^6)) δ 7.64 (d, $J = 7.3$ Hz, 2H), 7.55 (dd, $J = 22.6, 8.7$ Hz, 4H), 7.39 (t, $J = 7.4$ Hz, 2H), 7.34 (t, $J = 6.8$ Hz, 1H), 7.21 (s, 2H), 7.08 (s, 1H), 5.95 (s, 1H), 1.31 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, DMSO(d^6)) δ 154.47 (s), 139.40 (s), 138.99 (s), 137.71 (s), 134.04 (s), 130.83 (s), 130.31 (s), 129.18 (s), 129.00 (s), 128.78 (s), 127.05 (s), 124.18 (s), 74.08 (s), 34.95 (s), 30.63 (s).

4-(((4-Bromophenyl)sulfonyl)(phenyl)methyl)-2,6-di-tert-butylphenol (4af): [16] Pale yellow solid; 81% yield. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 7.61 (dd, $J = 7.7, 1.8$ Hz, 2H), 7.50–7.45 (m, 2H), 7.42–7.40 (m, 1H), 7.40–7.32 (m, 4H), 7.17 (s, 2H), 5.26 (s, 1H), 5.17 (s, 1H), 1.37 (s, 18H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 154.29 (s), 137.65 (s), 136.11 (s), 133.01 (s), 131.68 (s), 130.54 (s), 129.95 (s), 128.78 (s), 128.65 (s), 128.53 (s), 127.08 (s), 122.89 (s), 76.97 (s), 34.32 (s), 30.13 (s).

2,6-Di-tert-butyl-4-(((4-fluorophenyl)sulfonyl)(phenyl)methyl)phenol (4ag): [16] Pale yellow solid; 62% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.60 (dd, $J = 7.9, 1.2$ Hz, 2H), 7.58–7.53 (m, 2H), 7.38–7.28 (m, 3H), 7.21 (s, 2H), 7.04–6.95 (m, 2H), 5.26 (s, 1H), 5.18 (s, 1H), 1.37 (s, 18H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 164.46 (d, $J = 255.9$ Hz), 153.21 (s), 135.05 (s), 133.62 (s), 132.21 (s), 130.79 (d, $J = 9.5$ Hz), 128.91 (s), 127.70 (s), 127.55 (s), 126.00 (s), 122.05 (s), 114.63 (d, $J = 22.5$ Hz), 75.99 (s), 33.30 (s), 29.12 (s).

2,6-Di-tert-butyl-4-(phenyl((4-(trifluoromethyl)phenyl)sulfonyl)methyl)phenol (4ah): [16] Pale yellow solid; 82% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.69 (d, $J = 8.1$ Hz, 2H), 7.65–7.57 (m, 4H), 7.40–7.33 (m, 3H), 7.17 (s, 2H), 5.27 (s, 1H), 5.21 (s, 1H), 1.35 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, DMSO(d^6)) δ 154.68 (s), 142.95 (s), 139.58 (s), 134.06–133.29 (m), 133.82 (s), 130.51 (s), 130.13 (s), 129.22 (s), 129.06 (s), 127.28 (s), 126.44–126.15 (m), 123.96 (q, $J = 273.0$ Hz), 123.98 (s), 74.06 (s), 35.07 (s), 30.72 (s).

2,6-Di-tert-butyl-4-(phenyl((4-(trifluoromethoxy)phenyl)sulfonyl)methyl)phenol (4ai): Pale yellow solid; 84% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.61 (d, $J = 6.8$ Hz, 1H), 7.48 (d, $J = 8.5$ Hz, 1H), 7.37–7.32 (m, 1H), 7.31 (d, $J = 8.5$ Hz, 1H), 7.18 (s, 1H), 5.25 (s, 1H), 5.17 (s, 1H), 1.37 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, DMSO(d^6)) δ 154.48 (s), 152.04 (d, $J = 2.0$ Hz), 139.39 (s), 137.73 (s), 134.00 (s), 131.65 (s), 130.32 (s), 129.00 (s), 128.80 (s), 127.04 (s), 124.13 (s), 121.18 (s), 120.26 (q, $J = 258.2$ Hz), 74.07 (s), 34.93 (s), 30.59 (s); HRMS (ESI): m/z calcd for $\text{C}_{28}\text{H}_{31}\text{F}_3\text{O}_4\text{SNa}$ [$\text{M} + \text{Na}$] $^+$, 543.1785; found, 543.1787.

2,6-Di-tert-butyl-4-(((3-nitrophenyl)sulfonyl)(phenyl)methyl)phenol (4aj): Pale yellow solid; 86% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 8.38–8.32 (m, 1H), 8.30 (t, $J = 1.7$ Hz, 1H), 7.94 (d, $J = 7.7$ Hz, 1H), 7.63 (d, $J = 6.6$ Hz, 2H), 7.58 (t, $J = 8.0$ Hz, 1H), 7.42–7.33 (m, 3H), 7.23 (s, 2H), 5.30 (s, 1H), 5.24 (s, 1H), 1.36 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, CDCl_3) δ 154.56 (s), 147.81 (s), 140.94 (s), 136.49 (s), 134.26 (s), 132.33 (s), 129.99 (s), 129.66 (s), 128.97 (s), 128.93 (s), 127.49 (s), 127.07 (s), 124.48 (s), 122.32 (s), 77.12 (s), 34.35 (s), 30.14 (s); HRMS (ESI): m/z calcd for $\text{C}_{27}\text{H}_{31}\text{NO}_5\text{SNa}$ [$\text{M} + \text{Na}$] $^+$, 504.1817; found, 504.1815.

2,6-Di-tert-butyl-4-((naphthalen-1-ylsulfonyl)(phenyl)methyl)phenol (4ak): [16] Pale yellow solid; 52% yield. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 8.07 (d, $J = 1.2$ Hz, 1H), 7.85 (d, $J = 8.2$ Hz, 1H), 7.79 (dd, $J = 8.1, 5.2$ Hz, 2H), 7.67 (dd, $J = 7.8, 1.6$ Hz, 2H), 7.64–7.51 (m, 3H), 7.39–7.30 (m, 3H), 7.16 (s, 2H), 5.28 (s, 1H), 5.18 (s, 1H), 1.26 (s, 18H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ 153.06 (s), 134.88 (s), 134.37 (s), 133.97 (s), 132.31 (s), 130.81 (s), 130.02 (s), 129.01 (s), 128.23 (s), 128.02 (s), 127.67 (s), 127.47 (s), 127.42 (s), 126.74 (s), 126.34 (s), 126.04 (s), 122.65 (s), 122.38 (s), 75.89 (s), 33.18 (s), 29.01 (s).

2,6-Di-tert-butyl-4-(phenyl(thiophen-2-ylsulfonyl)methyl)phenol (4al): [16] Pale yellow solid; 76% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.63 (d, $J = 7.0$ Hz, 2H), 7.54 (d, $J = 3.7$ Hz, 1H), 7.40–7.30 (m, 3H), 7.28 (s, 3H), 7.01–6.89 (m, 1H), 5.30 (s, 1H), 5.26 (s, 1H), 1.38 (s, 18H). $^{13}\text{C-NMR}$ (151 MHz, DMSO(d^6)) δ 154.54 (s), 139.54 (s), 139.40 (s), 136.07 (s), 135.32 (s), 134.54 (s), 130.23 (s), 128.97 (s), 128.78 (s), 128.05 (s), 126.89 (s), 124.58 (s), 75.79 (s), 35.02 (s), 30.71 (s).

4-((Benzylsulfonyl)(phenyl)methyl)-2,6-di-tert-butylphenol (4am): [16] Pale yellow solid; 84% yield. $^1\text{H-NMR}$ (600 MHz, CDCl_3) δ 7.57 (dd, $J = 5.2, 3.3$ Hz, 2H), 7.42–7.29 (m, 8H), 7.17 (dd, $J = 7.9, 1.3$ Hz, 2H), 5.31 (s, 1H), 5.03 (s, 1H), 4.33–3.57 (m, 2H), 1.44 (s, 18H). $^{13}\text{C-NMR}$ (101 MHz, CDCl_3) δ

154.38 (s), 136.32 (s), 132.83 (s), 130.97 (s), 130.11 (s), 128.82 (s), 128.78 (s), 128.68 (d, $J = 2.0$ Hz), 128.07 (s), 126.88 (s), 122.93 (s), 71.81 (s), 58.13 (s), 34.48 (s), 30.30 (s).

3.2.2. Representative Procedure for General Reaction Procedure for Synthesis of Unsymmetrical Triarylmethane 7

To a solution of 2,6-di-*tert*-butyl-4-(phenyl(tosyl)methyl) phenol (45 mg, 0.10 mmol) in 1 mL DCE, KOH (5.6 mg, 0.10 mmol) and indole (14.06 mg, 0.12 mmol) were added. The mixture was stirred at 65 °C. The reaction was monitored by TLC. After complete reaction, the mixture was washed with water, dried over by anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was then purified by flash column chromatography on silica gel to afford the pure product 7.

2,6-Di-*tert*-butyl-4-((3*a*,7*a*-dihydro-1*H*-indol-3-yl)(phenyl)methyl)phenol (7): [41] Brown solid; 85% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.90 (s, 1H), 7.33 (d, $J = 8.1$ Hz, 1H), 7.25 (d, $J = 5.3$ Hz, 4H), 7.22 (d, $J = 8.1$ Hz, 1H), 7.18 (qd, $J = 5.3, 2.8$ Hz, 1H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.04 (s, 2H), 6.97 (t, $J = 7.5$ Hz, 1H), 6.58 (d, $J = 23.9$ Hz, 1H), 5.56 (s, 1H), 5.04 (s, 1H), 1.36 (s, 18H). ¹³C-NMR (151 MHz, CDCl₃) δ 152.91 (d, $J = 2.9$ Hz), 141.67 (s), 136.43 (d, $J = 2.7$ Hz), 135.80 (d, $J = 2.2$ Hz), 131.54 (s), 131.31 (s), 128.61 (d, $J = 2.9$ Hz), 128.43 (s), 127.04 (d, $J = 2.6$ Hz), 126.61 (d, $J = 3.0$ Hz), 125.21 (d, $J = 2.8$ Hz), 58.10 (s), 34.43 (s), 30.33 (s).

3.2.3. Representative Procedure for General Reaction Procedure for Synthesis of Unsymmetrical Gem-Diarylmethyl Thioether 8

To a solution of 2,6-di-*tert*-butyl-4-(phenyl(tosyl)methyl) phenol (45 mg, 0.1 mmol) in 1 mL methyl *tert*-butyl ether, Cs₂CO₃ (36 mg, 0.01 mmol) and TBAB (3.6 mg, 0.01 mmol) were added. Benzenethiol (13.68 μL, 0.12 mmol) was added to the solution dropwise, and the mixture was stirred at 80 °C. The reaction was monitored by TLC. After complete reaction, the mixture was concentrated in vacuo. The crude product was then purified by flash column chromatography on silica gel to afford the pure product 8.

2,6-Di-*tert*-butyl-4-(phenyl(phenylthio)methyl)phenol (8): [42] Colorless gummy liquid; 76% yield. ¹H-NMR (600 MHz, CDCl₃) δ 7.38 (d, $J = 7.4$ Hz, 2H), 7.20 (t, $J = 7.3$ Hz, 2H), 7.12 (t, $J = 7.0$ Hz, 3H), 7.10–7.00 (m, 5H), 5.35 (d, $J = 23.3$ Hz, 1H), 5.01 (d, $J = 23.1$ Hz, 1H), 1.29 (s, 18H). ¹³C-NMR (151 MHz, CDCl₃) δ 152.00 (s), 144.65 (s), 136.75 (s), 135.42 (s), 135.29 (s), 134.46 (s), 128.95 (s), 128.09 (s), 127.19 (s), 125.92 (s), 125.54 (s), 123.80 (s), 121.92 (s), 120.11 (s), 119.23 (s), 110.89 (s), 48.84 (s), 34.35 (s), 30.40 (s).

4. Conclusions

In summary, we developed the TBAB-promoted sulfa-1,6-conjugated addition of *para*-quinone methides with sulfonyl hydrazines in water. This reaction provides a green and sustainable method for direct synthesis of various unsymmetrical diarylmethyl sulfones with good functional group tolerance, scalability, and regioselectivity. Further transformation of the resulting diarylmethyl sulfones provides an efficient route to some functionalized molecules.

Supplementary Materials: The following are available online, the ¹H-NMR, ¹³C-NMR spectra of compounds 3aa–3ay and 4aa–4am, 7, 8; HRMS data of 4ad, 4ai and 4aj; crystal data of 4af are available as supporting data.

Author Contributions: Z.-Q.L. proposed the subject and designed the study, P.-S.Y. and D.-Q.L. carried out the chemical experiments, L.-D.Z. and S.-S.L. performed electrochemical data analysis, and X.-Y.G. wrote the article. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

THF	Tetrahydrofuran
DCE	Dichloroethane
DMSO	Dimethylsulfoxide
CTAB	Cetyltrimethyl Ammonium Bromide
TBAI	Tetrabutyl Ammonium Iodide
TEBAC	Triethylbenzyl Ammonium Chloride
TBAB	Tetrabutyl Ammonium Bromide
SDS	Sodium Dodecyl Sulfate
HRMS	High Resolution Mass Spectroscopy

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Sample Availability: Samples of the compounds compounds **3aa–3ay** and **4aa–4am** are available from the authors.



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