Metal-free, Acid/phosphine-induced Regioselective Thiolation of *para*-Quinone Methides with Sodium Aryl/alkyl Sulfinates

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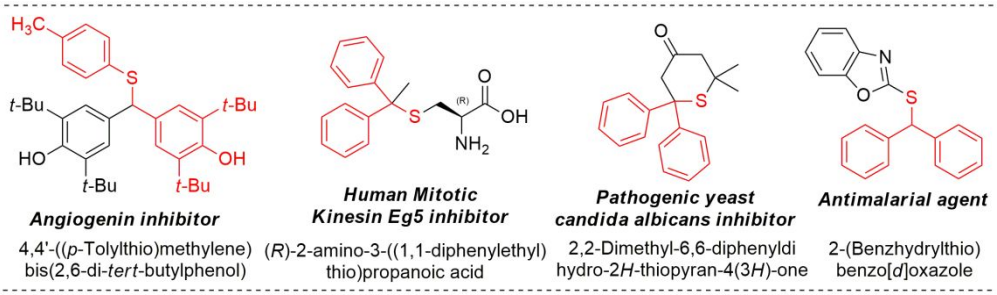
Abstract

A simple and efficient method for the regioselective thiolation of *para*-quinone methides with sodium aryl/alkyl sulfinates has been established by using an acid/phosphine-induced radical route under transition-metal-free conditions. A broad range of sodium aryl/alkyl sulfinates and *para*-quinone methides (*p*-QMs) are compatible for the reaction, giving the expected products with good to excellent yields. The control experiments were also performed to gain insights into the generation mechanism of thiyl radicals and hydrogen atom transfer process. This protocol provides a safe and feasible way for the formation of carbon-sulfur bonds.

Introduction

Owing to the unique antibacterial, anti-inflammatory and antimycobacterial activities, the construction of the C-S bonds for the synthesis and applications of diarylmethyl thioethers is of great interest in organic synthesis, materials science as well as in the pharmaceutical industry (**Scheme 1**).[1,2] The well-documented C-S bond forming methods for the synthesis of thioethers generally employed the nucleophilic substitution of aryl/alkyl halides with RS groups.[3] In addition, the introduction of S-H bonds into an unsaturated carbon-carbon bond is also an effective route to construct C-S bonds.[4] However, most of these protocols suffer from defects including the adoption of smell/air sensitive thiols, transition metal catalysts, oxidants (for the generation of thiyl radicals) and toxic organic solvents.

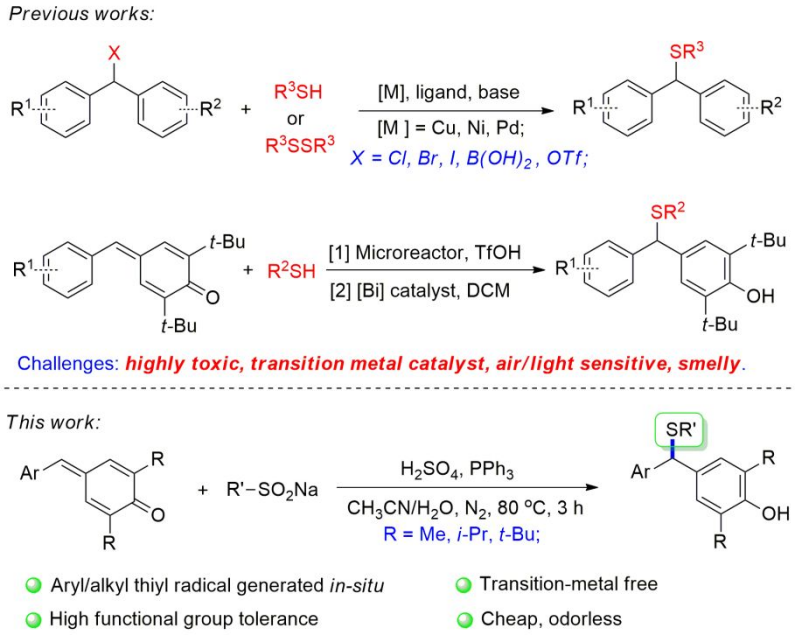
Scheme 1. Important diarylmethyl thioethers



Due to the unique bisvinylogous enone structure, *para*-quinone methides (*p*-QMs) are considered as electron-deficient alkenes, which have been widely employed in organic synthesis, especially in the 1,6-conjugated addition and intermolecular cyclization transformation.[5-8] Fan et al. established a novel and efficient catalytic asymmetric 1,6-conjugate addition/aromatization of *p*-QMs with malonates, oxindoles and glycine derivatives via the catalysis of small organic chiral amines.[9] In 2014, Jørgensen et al. disclosed a chiral secondary amine catalyzed asymmetric α-alkylation of aldehydes through the 1,6-conjugated addition of enamines with *p*-QMs, where a series of α-diarylmethyl-substituted aldehydes with two contiguous stereocenters were synthesized with good yields and excellent enantioselectivity.[10] In addition, the enantioselective 1,6-boration of *p*-QMs was achieved by Liao et al. through the catalysis of copper chloride and a chiral (2-(*tert*-butylsulfinyl)aryl) diisopropylphosphine ligand.[11] In the

presence of a chiral phosphoric acid, Li et al. discovered an efficient protocol for the asymmetric 1,6-conjugate addition of thioacetic acid to *p*-QMs.[12] Very recently, the Lewis acids and Bronsted acids catalyzed selective 1,6-conjugated addition of S-H bonds to *p*-QMs were realized by Anand et al. and Lu et al. under ambient temperature.[13]

Scheme 2. Methods for the synthesis of diaryl methyl thioethers from *p*-QMs



Thiyl radicals, which are at the center of some extremely efficient radical reactions for the synthesis of thioethers, have also attracted the interest of organic chemists.[14] Compared with the toxic and smelly thiophenol, sodium arylsulfinates are a kind of odorless, stable and easy-to-handle thiolation agents, which are undoubtedly considered as a safer and environmentally friendly reagents in organic synthesis. In 2017, Xu and Su et al. established an efficient protocol for the formation of C-S bonds via a by-product-promoted three-component coupling of alcohols with organic halides and thiourea.[15] In addition, a novel and convenient method was found by Lu and Yi et al. for the synthesis of alkyl/alkenyl sulfides and phosphonothioates from sodium arylsulfinates and alkynes, alkenes and *H*-phosphine oxides in aqueous system.[16] It should be noted that the aryl thiyl radicals were generated *in-situ* for the reaction. Although some elegant studies on the selective thiolation of carbon-carbon double bonds were achieved

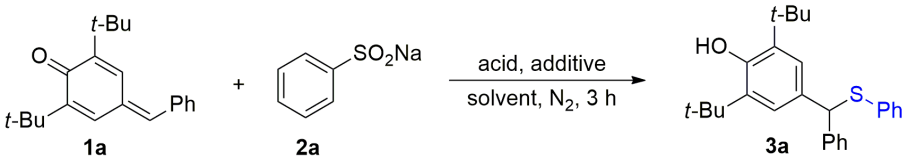
by these scientists, the use of *p*-QMs and sodium aryl/alkyl sulfinates as starting materials has not been reported. Herein, we demonstrate a simple and efficient method for the regioselective thiolation of *p*-QMs with sodium aryl/alkyl sulfinates by employing an acid/phosphine-induced radical route under transition-metal free conditions (**Scheme 2**).

Results and discussion

At the first stage of our study, we attempted to use PPh_3 and acid as the activation reagent for the reduction of S=O bond for the generation of aryl thiyl radical, followed by the attack on the C=C bond of *p*-QMs to realize the regioselective thiolation reaction. To test our initial hypothesis, the reaction of 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**1a**) and sodium benzenesulfinate (**2a**) was investigated to delineate the reaction parameters. The reaction of **1a** with **2a** was performed at 80 °C in H_2O under a N_2 atmosphere with the addition of triphenylphosphine and sulfuric acid, and the corresponding thiolation product of 2,6-di-*tert*-butyl-4-(phenyl(phenylthio)methyl)phenol (**3a**) was generated in 65% yield (**Table 1**, entry 1). To our delight, the mixed solvent system of 1,4-dioxane and H_2O (1.0 mL, *v*:*v* = 1:1) could afford the desired product **3a** in 82% yield (**Table 1**, entry 2). Besides 1,4-dioxane, other water-mixed solvent systems, such as EA/H_2O, CH_2Cl_2/H_2O, DMF/H_2O, THF/H_2O, toluene/H_2O, DMSO/H_2O and CH_3CN/H_2O were further investigated (**Table 1**, entries 3-9), and CH_3CN/H_2O gave the product in a preferable yield of 88%. The amounts of H_2SO_4 and PPh_3 used have the significant influences on the reaction. When we increased the amount of PPh_3 to 2.2 equivalents, **3a** could be generated in 99% yield. With the decrease of the use of PPh_3 or sulfuric acid, the yield of **3a** was decreased sharply (**Table 1**, entries 10-13). Additionally, it is worth noting that the reaction would not produce any products only in the presence of PPh_3 or sulfuric acid (**Table 1**, entries 14-15). In addition, we further screened other acids such as CF_3COOH, HCl, TsOH, CH_3COOH, H_3PO_4 and salicylic acid for the reaction (**Table 1**, entries 16-21). It is apparent that H_2SO_4 emerges as the best choice. Various reducing agents such as $(EtO)_2P(O)H$, Zn powder and Mn powder were also investigated (**Table 1**, entries 7 and 22-24). It is worth noting that only PPh_3 showed the positive results for the reduction of S=O bonds. When the reaction was operated at 60 °C, the desired product was only generated in 87% yield; but by further increasing the temperature from 80 °C to 100 °C, there are no

obvious effects on the reaction (**Table 1**, entries 25-26). Thus, the optimal reaction conditions are as follows: CH_3CN/H_2O (1.0 mL, *v*:*v* = 1:1), PPh_3 (2.2 eq), H_2SO_4 (2.0 eq), N_2, 80 °C, 3 h.

Table 1. Optimization of the reaction conditions [a]

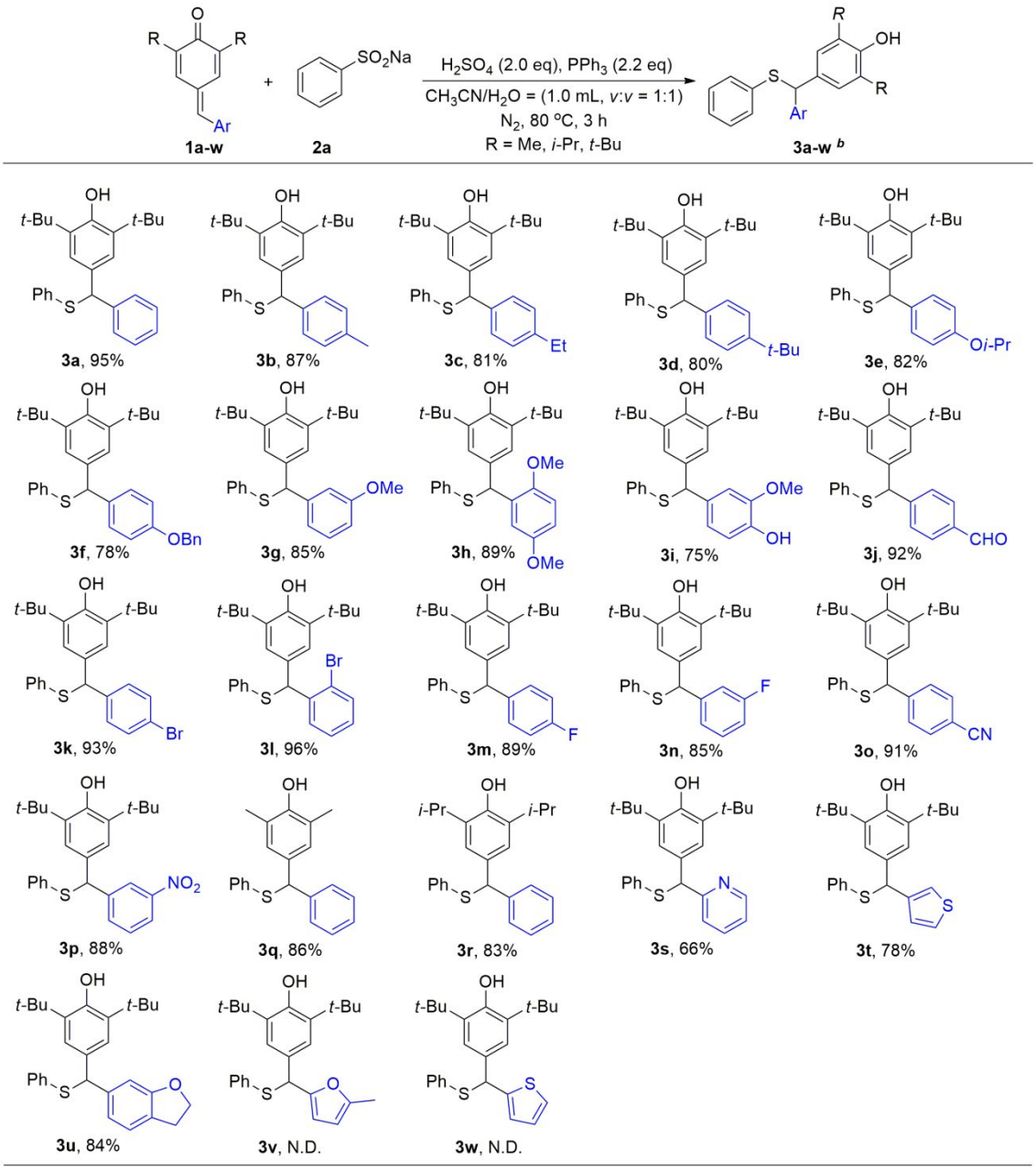


Entry	Solvent	Reductant	Acid	Yield [b]
1	H_2O	PPh_3 (2.0)	H_2SO_4	65%
2	1,4-dioxane/H_2O	PPh_3 (2.0)	H_2SO_4	82%
3	EA/H_2O	PPh_3 (2.0)	H_2SO_4	78%
4	CH_2Cl_2/H_2O	PPh_3 (2.0)	H_2SO_4	40%
5	DMF/H_2O	PPh_3 (2.0)	H_2SO_4	64%
6	THF/H_2O	PPh_3 (2.0)	H_2SO_4	86%
7	toluene/H_2O	PPh_3 (2.0)	H_2SO_4	61%
8	DMSO/H_2O	PPh_3 (2.0)	H_2SO_4	76%
9	CH_3CN/H_2O	PPh_3 (2.0)	H_2SO_4	88%
10	**CH_3CN/H_2O**	**PPh_3 (2.2)**	**H_2SO_4**	**99%**
11	CH_3CN/H_2O	PPh_3 (1.0)	H_2SO_4	47%
12	CH_3CN/H_2O	PPh_3 (2.2)	H_2SO_4	73% [c]
13	CH_3CN/H_2O	PPh_3 (2.2)	H_2SO_4	56% [d]
14	CH_3CN/H_2O	PPh_3 (2.2)	-	0%
15	CH_3CN/H_2O	-	H_2SO_4	0%
16	CH_3CN/H_2O	PPh_3 (2.2)	CF_3COOH	70%
17	CH_3CN/H_2O	PPh_3 (2.2)	HCl	80%
18	CH_3CN/H_2O	PPh_3 (2.2)	TsOH	25%
19	CH_3CN/H_2O	PPh_3 (2.2)	CH_3COOH	54%
20	CH_3CN/H_2O	PPh_3 (2.2)	H_3PO_4	91%
21	CH_3CN/H_2O	PPh_3 (2.2)	Salicylic acid	82%
22	CH_3CN/H_2O	$(EtO)_2P(O)H$ (2.2)	H_2SO_4	22%
23	CH_3CN/H_2O	Zn (2.2)	H_2SO_4	trace
24	CH_3CN/H_2O	Mn (2.2)	H_2SO_4	trace
25	CH_3CN/H_2O	PPh_3 (2.2)	H_2SO_4	87% [e]
26	CH_3CN/H_2O	PPh_3 (2.2)	H_2SO_4	99% [f]

[a] Reactions were carried out with 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**1a**, 0.2 mmol), sodium benzenesulfinate (**2a**, 1.2 eq), reductant (x eq), and acid (2.0 eq) in solvent (1.0 mL; for the mixed solvent system, *v* : *v* = 1:1), under a N_2 atmosphere stirred for 3 h at 80 °C.[b] Yield was determined by GC analysis, using dodecane as the internal standard. [c] H_2SO_4 (1.0 eq). [d] H_2SO_4 (0.5 eq). [e] 60 °C. [f] 100 °C.

Table 2. Substrate scope of *p*-QMs

a



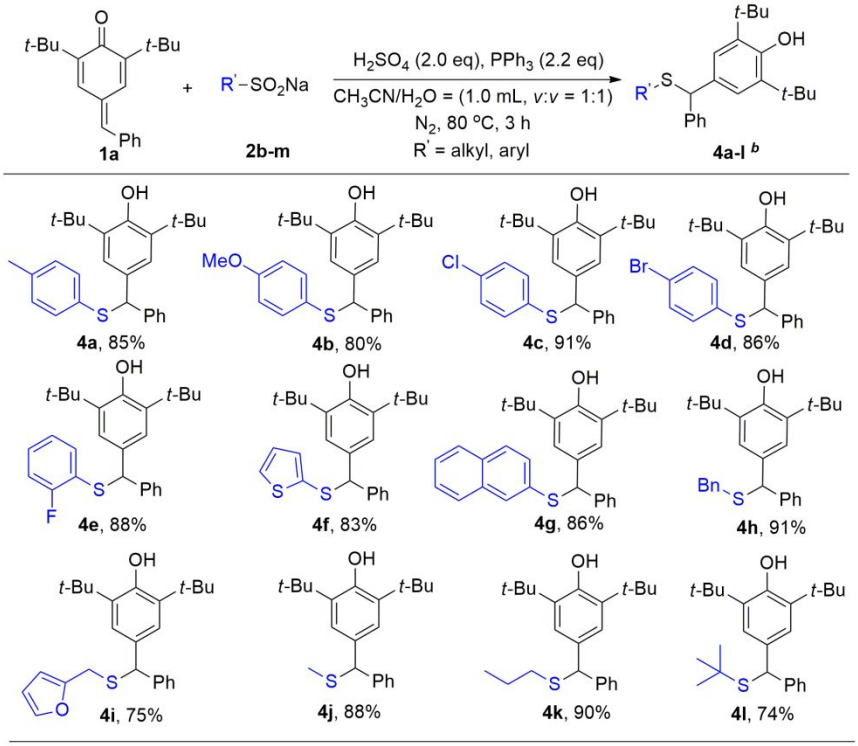
[a] Reaction conditions: sodium benzenesulfinate (0.24 mmol), *p*-QMs compound (0.2 mmol), PPh_3 (0.44 mmol), H_2SO_4 (0.4 mmol), CH_3CN/H_2O (1.0 mL, *v*:*v* = 1:1), N_2, 80 °C, 3 h. [b] Isolated yields. [c] GC yield.

As shown in **Table 2**, the acid/phosphine-induced regioselective thiolation of *para*-quinone methides with sodium benzenesulfinate leading to 2,6-di-*tert*-butyl-4-(aryl(phenylthio)methyl)phenols can be applied to different kinds of *p*-QMs. It is clear that 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone (1**a**), 2,6-di-*tert*-butyl-4-(4-methylbenzylidene)cyclo-hexa-2,5-dienone (**1b**), 2,6-di-*tert*-butyl-4-(4-ethylbenzylidene) cyclohexa-2,5-dienone (**1c**) and 2,6-di-*tert*-butyl-4-(4-(*tert*-

butyl)benzylidene)cyclo-hexa-2,5-dienone (**1d**) can react efficiently with sodium benzenesulfinate (**2a**) under the optimized reaction conditions, affording the corresponding thiolation products of **3a**-**3d** in 80-95% isolated yields. In addition, when 2,6-di-*tert*-butyl-4-(4-*iso*-propoxybenzylidene)cyclohexa-2,5-dienone (**1e**), 4-(4-(benzyloxy)benzylidene)-2,6-di-*tert*-butylcyclo-hexa-2,5-dienone (**1f**), 2,6-di-*tert*-butyl-4-(3-methoxybenzylidene)cyclohexa-2,5-dienone (**1g**), and 2,6-di-*tert*-butyl-4-(2,5-dimethoxybenzylidene) cyclohexa-2,5-dienone (**1h**) were employed as the substrates for the reaction, the desired thiolation products were obtained in 78-89% yields. To our surprise, 2,6-di-*tert*-butyl-4-((4-hydroxy-3-methoxyphenyl)(phenylthio)methyl)phenol (**3i**) and 4-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(phenylthio)methyl) benzaldehyde (**3j**) were synthesized with 75% and 92% yields through the 1,6-conjugated addition reaction of 2,6-di-*tert*-butyl-4-(4-hydroxy-3-methoxybenzylidene) cyclohexa-2,5-dienone (**1i**) and 4-((3,5-di-*tert*-butyl-4-oxocyclohexa-2,5-dien-1ylidene)methyl) benzaldehyde (**1j**) with **2a**, where the hydroxyl and aldehyde substituents remained to be there after the reaction without the protection. Furthermore, various kinds of *p*-QMs containing electron-withdrawing groups (e.g., bromo, fluoro, cynao and nitro, **1k**-**1p**) on the aryl ring also exhibit high reactivities toward the thiolation/1,6-conjugated addition process, affording the corresponding products in 85-96% yields. For most cases, electron-donating or electron-withdrawing groups which are located on the aryl ring of *p*-QMs do not change the yields of the products significantly. It is worth noting that **3q** and **3r** could be synthesized from 4-benzylidene-2,6-dimethylcyclohexa-2,5-dienone (**1q**) and 4-benzylidene-2,6-diisopropylcyclohexa-2,5-dienone (**1r**) with **2a** in 86% and 83% yields under the present reaction conditions, respectively. Interestingly, when 2,6-di-*tert*-butyl-4-(pyridin-2-ylmethylene)cyclohexa-2,5-dienone (**1s**), 2,6-di-*tert*-butyl-4-(thiophen-3-ylmethylene)cyclohexa-2,5-dienone (**1t**), 2,6-di-*tert*-butyl-4-((2,3-dihydrobenzofuran-6-yl)methylene)cyclohexa-2,5-dienone (**1u**) were used as the substrates for the reaction, the corresponding thiolation products of **3s**-**3u** could be generated in 66-84% yields. However, the *ortho*-heteroatom substituted heterocyclic *p*-QMs such as 2,6-di-*tert*-butyl-4-((5-methylfuran-2-yl)methylene)cyclohexa-2,5-dienone (**1v**) and 2,6-di-*tert*-butyl-4-(thiophen-2-ylmethylene)cyclohexa-2,5-dienone (**1w**) showed the negative results toward the reaction, and this

phenomenon may be ascribed to the fact that the O- and S-atoms in the *ortho*-heterocyclic ring could interrupt the reduction path of sodium benzenesulfinate in the reaction.

Table 3. Substrate scope of sodium aryl/alkyl sulfinates [a]

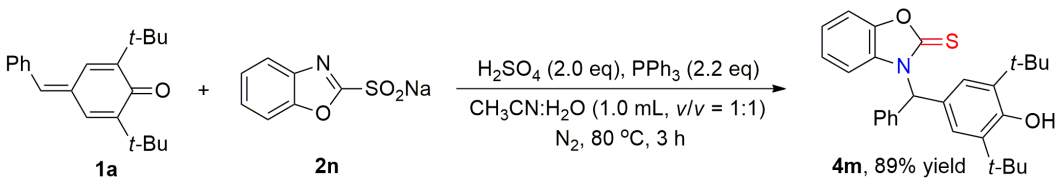


[a] Reaction conditions: 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**1a**, 0.2 mmol), sodium aryl/alkyl sulfinate (**2**, 0.24 mmol), PPh_3 (0.44 mmol), H_2SO_4 (0.4 mmol), CH_3CN/H_2O (1.0 mL, *v*:*v* = 1:1), N_2, 80 °C, 3 h. [b] Isolated yields.

As depicted in **Table 3**, a range of substituted sodium aryl/alkyl sulfinates (**2b**-**2m**) were screened under the optimized reaction conditions with **1a**. It is clear that sodium aryl sulfinates bearing electron-donating groups such as sodium 4-methylbenzenesulfinate (**2b**) and sodium 4-methoxybenzenesulfinate (**2c**), exhibit high reactivity toward 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**1a**), affording the expected thiolation products of **4a** and **4b** in 85% and 80% yields, respectively. Additionally, the electron-withdrawing groups substituted in the aryl ring of sodium arylsulfinates, such as sodium 4-chlorobenzenesulfinate (**2d**), sodium 4-bromobenzenesulfinate (**2e**) and sodium 2-fluorobenzenesulfinate (**2f**), also showed satisfactory results, giving the desired thiolation products of

4c-**4e** with 86-91% yields. When sodium thiophene-2-sulfinate (**2g**) and sodium naphthalene-2-sulfinate (**2h**) were employed, the corresponding products of 2,6-di-*tert*-butyl-4-(phenyl(thiophen-2-ylthio)methyl)phenol (**4f**) and 2,6-di-*tert*-butyl-4-((naphthalen-2-ylthio)(phenyl)methyl)phenol (**4g**) could be synthesized in 83% and 86% yields. Notably, different kinds of sodium alkyl sulfinates such as sodium phenylmethanesulfinate (**2i**), sodium furan-2-ylmethanesulfinate (**2j**), sodium methanesulfinate (**2k**), sodium propane-1-sulfinate (**2l**) and sodium 2-methylpropane-2-sulfinate (**2m**) are also appropriate for this transformation to afford the thiolation products of **4h**-**4l** in moderate to good yields.

Scheme 3. Rearrangement/1,6-conjugated addition of sodium benzo[*d*]oxazole-2-sulfinate to 2a



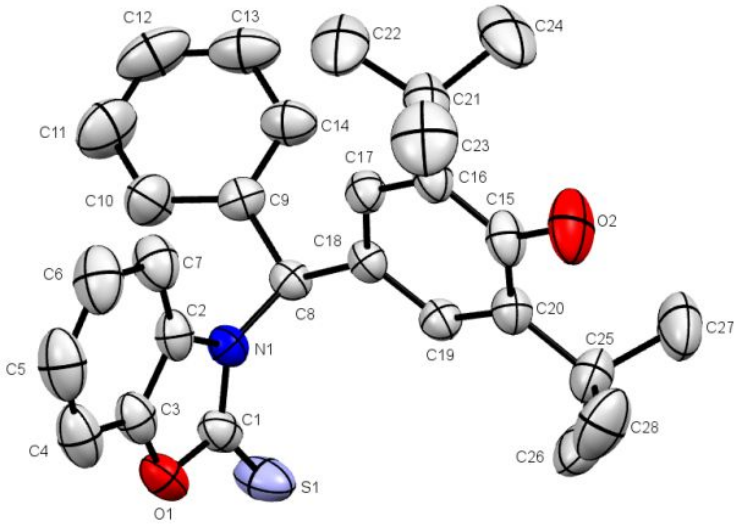
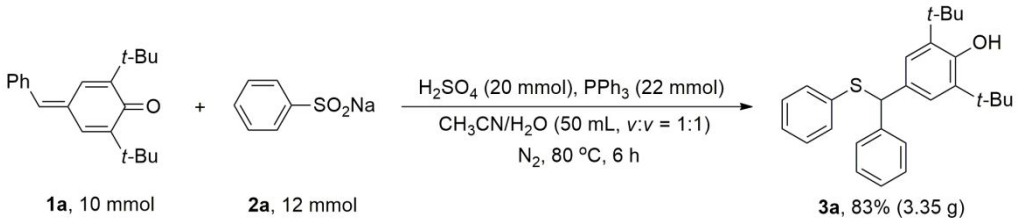


Figure 1. ORTEP drawing of compound **4m**.[18] Hydrogen atoms are omitted for clarity; ellipsoids are drawn at 50% probability. Selected bond lengths [Å] and angles [deg]: N1-C1 1.360(3), N1-C2 1.416(3), N1-C8 1.478(3), C1-S1 1.646(2), C1-O1 1.371(3), C15-O2 1.382(3); C9-C8-C18 116.4(2), N1-C8-C18 109.5(2), C8-N1-C1 123.1(2), C8-N1-C2 127.5(2), N1-C1-S1 108.3(2), O1-C1-S1 122.2(2), N1-C1-O1 108.3(2).

To our surprise, when sodium benzo[*d*]oxazole-2-sulfinate (**2n**) was used as the thiolation reagent for this transformation, 3-((3,5-di-*tert*-butyl-4-hydroxyphenyl)(phenyl)methyl)benzo[d]oxazole-2(3H)-

thione (**4m**) was generated in 89% yield as the rearrangement/1,6-conjugated addition product for the reaction. It is deduced that the benzo[*d*]oxazole-2-thione radical is much stabler than the benzo[d]oxazole-2-thiol radical, which was formed *in-situ* through the intramolecular rearrangement of the benzo[*d*]oxazole-2-thiol radical during the reaction, thus leading to the synthesis of an amination product (**Scheme 3**, **Figure 1**).

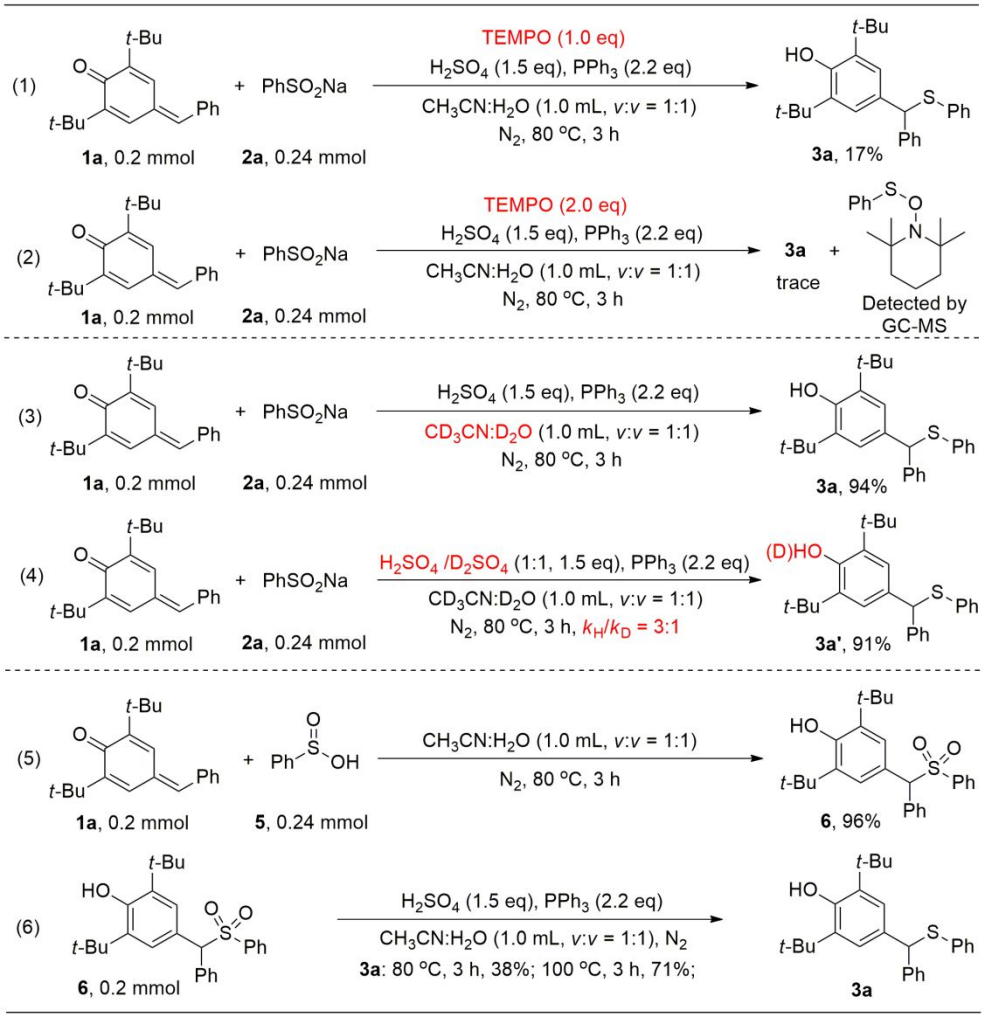
Scheme 4. Large-scale synthesis of 3a



In order to demonstrate the practical application of this protocol, we conducted a large-scale reaction of 4-benzylidene-2,6-di-*tert*-butylcyclohexa-2,5-dienone (**1a**, 10 mmol) with sodium benzenesulfinate (**2a**, 12 mmol) and generated **3a** in 83% yield (3.35 g, **Scheme 4**). In addition, a series of control experiments were performed under the optimized reaction conditions (**Scheme 5**). When the reaction was conducted with the addition of a radical scavenger 2,2,6,6-tetramethylpiperidine *N*-oxyl (TEMPO), there was only trace amounts of **3a** detected after the reaction (**Scheme 5**, eqs 1 and 2). This result proves that a phenyl thiyl radical may be produced during the reaction. When acetonitrile-d_3 and D_2O were employed as a mixed solvent for the reaction, **3a** was generated in 94% yield, and there was no deuterization signal found for **3a**. It is deduced that the hydrogen atom for the thiolation/1,6-conjugated product was derived from H_2SO_4. Based on this result, we further performed a kinetic isotope effect (KIE) experiment between H_2SO_4 and D_2SO_4 for this reaction. A KIE (k_H/k_D) constant was determined as 3.0 (**Scheme 5**, eqs 3 and 4). When benzenesulfinic acid (**5**) was adopted as the substrate to react with *p*-QMs, the corresponding 1,6-conjugated adduct of 2,6-di-*tert*-butyl-4-(phenyl(phenylsulfonyl)methyl) phenol (**6**) was generated in 96% yield. In the presence of sulfuric acid and PPh_3, the S=O bonds in **6**

could be reduced efficiently to afford **3a** in 38% (80 °C, 3 h) and 71% (100 °C, 3 h) yields, respectively (**Scheme 5**, eqs 5 and 6).

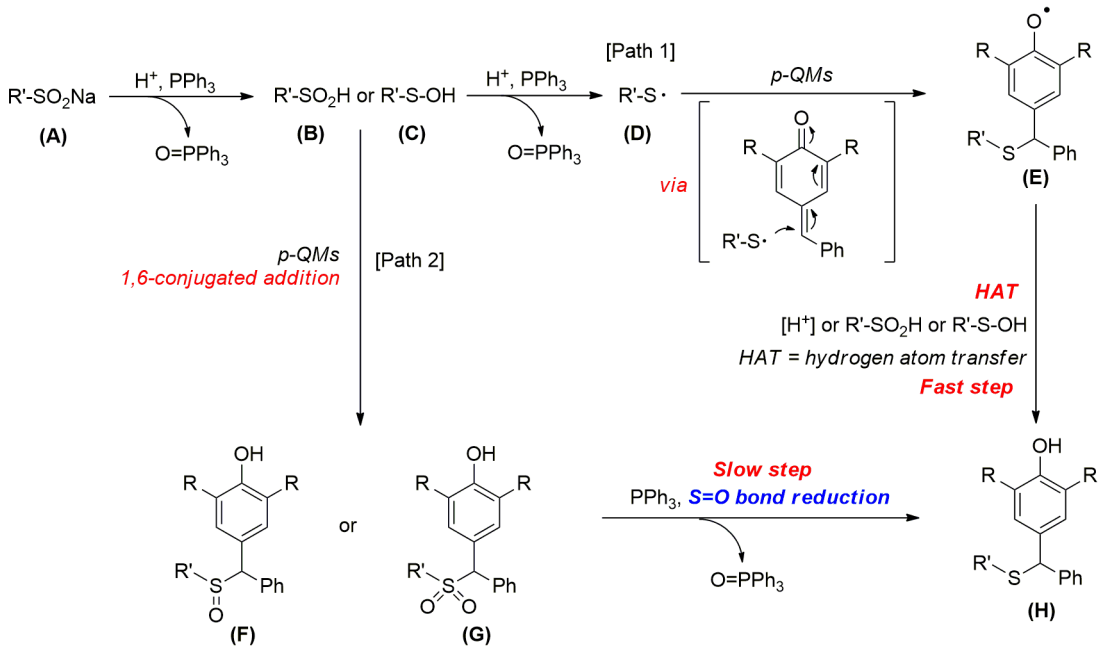
Scheme 5. Control experiments for the reaction mechanism



According to the above results, a plausible mechanism for the stereoselective thiolation of *p*-QMs compound with sodium aryl/alkyl sulfinates is proposed in **Scheme 6**. The present reaction might involve two possible paths. In the presence of sulfuric acid and PPh_3, the corresponding thiyl radical (**D**) could be formed through the acidification and reduction of sodium aryl/alkyl sulfinate (**A**). Then the thiyl radical (**D**) proceed the radical addition at the olefinic moiety of *p*-QMs with the generation of the intermediate radical **E**. Through the assistance of an acid, **E** could undergo the hydrogen atom transfer process to yield the final 1,6-conjugated adduct (Path 1). On the other hand, the 1,6-conjugated addition products of **F** and **G** could be synthesized firstly through the reaction of benzenesulfinic acid (**B**) and

phenylsulfanol (**C**) with *p*-QMs. In the presence of sulfuric acid and PPh_3, the final product can be formed correspondingly through the selective reduction of S=O bonds. Triphenylphosphine oxide was generated as the by product for the reaction (Path 2). According to the control experiment results in **Scheme 4** (eqs 5 and 6), it is deduced that Path 1 might be the fast step for the reaction.

Scheme 6. A plausible mechanism



Conclusions

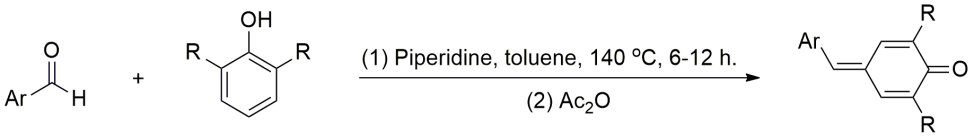
In summary, we developed an convenient and highly efficient method for the synthesis of diaryl methyl thioethers through the 1,6-conjugate addition of sodium aryl/alkyl sulfinates with *p*-QMs. The approach avoids the use of highly toxic thiophenols and transition metals, and the reaction can be performed under mild conditions. Through the control experiments, this transformation might be achieved with two different paths. To the best of our knowledge, the regioselective thiolation of *p*-QMs with sodium aryl/alkyl sulfinates has not been exploited previously, and the salient features of this transformation include its broad substrate scope, absence of transition metals, and good regioselectivity. This protocol also exhibits high potential for the construction of biologically active diarylmethyl thioethers.

Experimental Section

General Considerations:

All solvents used in the reactions were freshly distilled. The other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen unless specified otherwise. ^{1}H (400 MHz) and $^{13}C\{^{1}H\}$ (100 MHz) were recorded on a 400 MHz spectrometer in $CDCl_3$. ^{1}H NMR chemical shifts were reported using TMS as the internal standard while $^{13}C\{^{1}H\}$ NMR chemical shifts were reported relative to $CDCl_3$. The electron ionization method was used for HRMS measurements, and the mass analyzer type was double-focusing.

General procedure for the preparation of *para*-quinone methides (*p*-QMs):



According to the reported procedure,[8f] 1.0 equiv of 2,6-di-*tert*-butylphenol and 1.0 equiv of aldehyde were dissolved in toluene (0.25 M) and the mixture was heated to 140 °C in a Dean-Stark apparatus (oil bath). Piperidine (2.0 equiv) was added dropwise over 1 h and the reaction mixture was refluxed for 6-12 h. After cooling just below the boiling point of the mixture, acetic anhydride (2.0 equiv) was added and stirring was continued for 15 min. Then the reaction mixture was poured into the ice-water, extracted with DCM, dried over Na_2SO_4, the solvent evaporated and the residue dried *in vacuo*. Pure *p*-QMs product was obtained by passing the crude product through a short silica gel column using *n*-hexane as eluent. Some other substituents (*e.g.*, -Cl, -OMe, -Ph) in substituted *p*-QMs failed to get the isolated products in the reactions of 2,6-dimethoxyphenol, 2,6-dichlorophenol and 2,6-diphenylphenol with benzaldehyde.

General procedure:

A mixture of *para*-quinone methides (*p*-QMs) (0.2 mmol), RSO_2Na (0.24 mmol, 1.2 eq), H_2SO_4 (0.4 mmol, 2.0 eq) and PPh_3 (0.44 mmol, 2.2 eq) were dissolved in CH_3CN/H_2O (1.0 mL, v : v = 1:1) under a N_2 atmosphere stirred for 3.0 h at 80 °C in an oil bath. Upon completion of the reaction, the mixture

was concentrated under vacuum. Removal of the solvent under a reduced pressure gave the crude product; pure product was obtained by passing the crude product through a short silica gel column using *n*-hexane/EtOAc (80:1-5:1) as eluent.

2,6-Di-tert-butyl-4-(pyridin-2-ylmethylene)cyclohexa-2,5-dienone (1s): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **2s** (2.2 g, 7.5 mmol, 75%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 8.72-8.74 (m, 2H), 7.70-7.74 (m, 1H), 7.39-7.41 (m, 1H), 7.20-7.23 (m, 1H), 6.95-6.98 (m, 2H), 1.34 (d, *J* = 5.4 Hz, 18H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 186.7 (s), 155.2 (s), 150.1 (s), 149.8 (s), 148.5 (s), 138.3 (s), 136.5 (s), 135.5 (s), 134.5 (s), 129.2 (s), 127.2 (s), 35.6 (s), 35.1 (s), 29.7 (s), 29.6 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{20}H_{26}NO$ $[M+H]^+$: 296.2014, found: 296.2011.

2,6-Di-tert-butyl-4-(thiophen-3-ylmethylene)cyclohexa-2,5-dienone (1t): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **2t** (2.4 g, 7.9 mmol, 79%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.65-7.66 (m, 1H), 7.52-7.53 (m, 1H), 7.42-7.44 (m, 1H), 7.31-7.32 (m, 1H), 7.08 (s, 1H), 6.98-6.99 (m, 1H), 1.33 (d, *J* = 3.4 Hz, 18H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 186.4 (s), 149.2 (s), 147.6 (s), 137.8 (s), 135.8 (s), 135.3 (s), 130.9 (s), 128.7 (s), 128.6 (s), 127.5 (s), 126.9 (s), 35.5 (s), 35.0 (s), 29.6 (s), 29.5 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{19}H_{25}OS$ $[M+H]^+$: 301.1626, found: 301.1625.

2,6-Di-tert-butyl-4-((2,3-dihydrobenzofuran-6-yl)methylene)cyclohexa-2,5-dienone (1u): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **2u** (2.6 g, 7.6 mmol, 76%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.46-7.47 (m, 1H), 7.25 (s, 1H), 7.18-7.19 (m, 1H), 7.03 (s, 1H), 6.90-6.91 (m, 1H), 6.76-6.78 (m, 1H), 4.56 (t, *J* = 8.7 Hz, 2H), 3.17 (t, *J* = 8.7 Hz, 2H), 1.24 (d, *J* = 5.3 Hz, 18H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 186.5 (s), 161.5 (s), 148.8 (s), 147.0 (s), 143.4 (s), 135.5 (s), 131.7 (s), 130.1 (s), 128.8 (s), 128.2 (s), 127.9 (s), 127.4 (s), 109.9 (s) , 71.9 (s), 35.4 (s), 35.0 (s), 29.6 (s), 29.5 (s), 29.4 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{23}H_{29}O_2$ $[M+H]^+$: 337.2168, found: 337.2166.

2,6-Di-tert-butyl-4-((5-methylfuran-2-yl)methylene)cyclohexa-2,5-dienone (1v): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **2v** (2.5 g, 8.4 mmol, 84%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 8.17-8.18 (m, 1H), 6.91-6.92 (m, 1H), 6.60 – 6.65 (m, 2H), 6.17-6.17 (m, 1H), 2.42 (s, 3H), 1.35 (d, *J* = 19.1 Hz, 18H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 185.8 (s), 157.2 (s), 151.7 (s), 148.5 (s), 147.1 (s), 135.0 (s), 128.8 (s), 127.2 (s), 126.4 (s), 120.4 (s), 109.6 (s), 35.5 (s), 35.0 (s), 29.6 (s), 29.5 (s) 14.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{20}H_{27}O_2$ $[M+H]^+$: 299.2011, found: 299.2007.

2,6-Di-tert-butyl-4-(thiophen-2-ylmethylene)cyclohexa-2,5-dienone (1w): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **2w** (2.3 g, 7.8 mmol, 78%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.86-7.87 (m, 1H), 7.55-7.56 (m, 1H), 7.32-7.33 (m, 1H), 7.19 (s, 1H), 7.10-7.12 (m, 1H), 6.95-6.96 (m, 1H), 1.35 (d, *J* = 19.1 Hz, 18H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 186.2 (s), 149.3 (s), 147.4 (s), 139.3 (s), 135.3 (s), 134.2 (s), 134.0 (s), 131.2 (s), 129.0 (s), 127.9 (s), 127.0 (s), 35.7 (s), 35.0 (s), 29.6 (s), 29.5 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{19}H_{25}OS$ $[M+H]^+$: 301.1626, found: 301.1623.

2,6-Di-tert-butyl-4-(phenyl(phenylthio)methyl)phenol (3a): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **3a** (76.8 mg, 0.19 mmol, 95%) as a yellow oil.[13a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.45-7.47 (m, 2H), 7.26-7.30 (m, 2H), 7.19-7.22 (m, 3H), 7.11-7.17 (m, 5H), 5.45 (s, 1H), 5.11 (s, 1H), 1.37 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.9 (s), 141.6 (s), 136.4 (s), 135.7 (s), 131.4 (s), 131.1 (s), 128.6 (s), 128.5 (s), 128.4 (s), 127.0 (s), 126.6 (s), 125.1 (s), 57.9 (s), 34.4 (s), 30.3 (s).

2,6-Di-tert-butyl-4-((phenylthio)(p-tolyl)methyl)phenol (3b): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **3b** (72.8 mg, 0.174 mmol, 87%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.26-7.28 (m, 2H), 7.12-7.14 (m, 2H), 7.00-7.08 (m, 7H), 5.35 (s, 1H), 5.02 (s, 1H), 2.21 (s, 3H), 1.29 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.9 (s), 138.6 (s), 136.6 (s), 135.6 (s), 131.7 (s), 131.0 (s), 129.2 (s), 128.6 (s), 128.5 (s), 128.2 (s), 126.5 (s), 125.1 (s), 57.7 (s), 34.4 (s), 30.3 (s), 21.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{28}H_{35}OS$ $[M+H]^+$: 419.2409, found: 419.2405.

2,6-Di-tert-butyl-4-((phenylthio)(p-tolyl)ethyl)phenol (3c): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **3c** (70.0 mg, 0.162 mmol, 81%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.28-7.30 (m, 2H), 7.12-7.14 (m, 2H), 7.02-7.08 (m, 7H), 5.35 (s, 1H), 5.02 (s, 1H), 2.49-2.55 (m, 2H), 1.29 (s, 18H), 1.12 (t, *J* = 7.6Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.8 (s), 143.0 (s), 138.8 (s), 136.6 (s), 135.6 (s), 131.7 (s), 131.0 (s), 128.6 (s), 128.2 (s), 128.0 (s), 126.5 (s), 125.1 (s), 57.7 (s), 34.4 (s), 30.3 (s), 28.5 (s), 21.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{29}H_{37}OS$ $[M+H]^+$: 433.2565, found: 433.2560.

2,6-Di-tert-butyl-4-((4-(tert-butyl)phenyl)(phenylthio)methyl)phenol (3d): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 60:1) gave product **3d** (73.6 mg, 0.16 mmol, 80%) as a colorless oil.[13a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.37-7.39 (m, 2H), 7.29-7.31 (m, 2H), 7.19-7.23 (m, 2H), 7.11-7.17 (m, 5H), 5.41 (s, 1H), 5.10 (s, 1H), 1.37 (s, 18), 1.29 (s, 9H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.8 (s), 149.9 (s), 138.6 (s), 136.6 (s), 136.0 (s), 131.7 (s), 131.2 (s), 128.7 (s), 127.9 (s), 126.5 (s), 125.4 (s), 125.2 (s), 57.7 (s), 34.4 (s), 31.4 (s), 30.3 (s), 30.2 (s).

2,6-Di-tert-butyl-4-((4-isopropoxyphenyl)(phenylthio)methyl)phenol (3e): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 40:1) gave product **3e** (75.8 mg, 0.164 mmol, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.26-7.29 (m, 2H), 7.12-7.15 (m, 2H), 7.04-7.10 (m, 5H), 6.72-6.74 (m, 2H), 5.33 (s, 1H), 5.04 (s, 1H), 4.41-4.46 (m, 1H), 1.30 (s, 18H), 1.22 (d, *J* = 6.4 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 156.8 (s), 152.8 (s), 136.5 (s), 135.6 (s), 133.5 (s), 131.7 (s), 131.1 (s), 129.4 (s), 128.6 (s), 126.5 (s), 125.1 (s), 115.7 (s), 69.9 (s), 57.3 (s), 34.4 (s), 30.3 (s), 22.1 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{30}H_{39}O_2S$ $[M+H]^+$: 463.2671, found: 463.2668.

4-((4-(Benzyloxy)phenyl)(phenylthio)methyl)-2,6-di-tert-butylphenol (3f): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 50:1) gave product **3f** (79.6 mg, 0.156 mmol, 78%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.22-7.31 (m, 7H), 7.04-7.13 (m, 7H), 6.80-6.82 (m, 2H), 5.34 (s, 1H), 5.03 (s, 1H), 4.93 (s, 2H), 1.29 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 157.8 (s), 152.9 (s), 137.0 (s), 136.5 (s), 135.7 (s),

134.0 (s), 131.7 (s), 131.1 (s), 129.5 (s), 128.6 (s), 128.5 (s), 128.0 (s), 127.6 (s), 126.5 (s), 125.1 (s), 114.7 (s), 70.0 (s), 57.3 (s), 34.4 (s), 30.3 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{34}H_{39}O_2S$ $[M+H]^+$: 511.2671, found: 511.2668.

2,6-Di-tert-butyl-4-((3-methoxyphenyl)(phenylthio)methyl)phenol (3g): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 10:1) gave product **3g** (73.8 mg, 0.17 mmol, 85%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$, 25 ^oC, TMS): δ = 7.19-7.23 (m, 3H), 7.11-7.17 (m, 5H), 7.03-7.07 (m, 2H), 6.73-6.76 (m, 1H), 5.42 (s, 1H), 5.12 (s, 1H), 3.76 (s, 3H), 1.37 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 ^oC, TMS): δ = 159.6 (s), 152.9 (s), 143.2 (s), 136.4 (s), 135.7 (s), 131.3 (s), 131.1 (s), 129.4 (s), 128.7 (s), 126.6 (s), 125.1 (s), 120.8 (s), 113.9 (s), 112.7 (s), 57.9 (s), 55.2 (s), 34.4 (s), 30.3 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{28}H_{35}O_2S$ $[M+H]^+$: 435.2358, found: 435.2354.

2,6-Di-tert-butyl-4-((2,4-dimethoxyphenyl)(phenylthio)methyl)phenol (3h): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 10:1) gave product **3h** (82.6 mg, 0.178 mmol, 89%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$, 25 ^oC, TMS): δ = 7.22-7.23 (m, 1H), 7.13-7.15 (m, 4H), 6.99-7.08 (m, 3H), 6.60-6.67 (m, 2H), 5.90 (s, 1H), 5.01 (s, 1H), 3.63 (d, *J* = 10.0 Hz, 6H), 1.30 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 ^oC, TMS): δ = 153.7 (s), 152.8 (s), 150.9 (s), 136.9 (s), 135.5 (s), 131.4 (s), 131.1 (s), 130.2 (s), 128.6 (s), 126.1 (s), 125.2 (s), 114.8 (s), 113.0 (s), 112.1 (s), 56.4 (s), 55.8 (s), 49.6 (s), 34.4 (s), 30.3 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{29}H_{37}O_3S$ $[M+H]^+$: 465.2463, found: 465.2460.

2,6-Di-tert-butyl-4-((4-hydroxy-3-methoxyphenyl)(phenylthio)methyl)phenol (3i): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 10:1) gave product **3i** (67.5 mg, 0.15 mmol, 75%) as a colorless oil. ^1H NMR (400 MHz, $CDCl_3$, 25 ^oC, TMS): δ = 7.21-7.23 (m, 2H), 7.12-7.18 (m, 5H), 7.00-7.01 (m, 1H), 6.90-6.93 (m, 1H), 6.81-6.83 (m, 1H), 5.57 (s, 1H), 5.40 (s, 1H), 5.13 (s, 1H), 3.82 (s, 3H), 1.38 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 ^oC, TMS): δ = 152.9 (s), 146.4 (s), 144.6 (s), 136.4 (s), 135.6 (s), 133.5 (s), 131.6 (s), 131.3 (s), 128.6 (s), 126.6 (s), 125.0 (s), 121.4 (s), 114.2 (s), 110.9 (s), 57.8 (s), 55.9 (s), 34.4 (s), 30.3 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{28}H_{35}O_3S$ $[M+H]^+$: 451.2307, found: 451.2305.

4-((3,5-Di-tert-butyl-4-hydroxyphenyl)(phenylthio)methyl)benzaldehyde (3j): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 30:1) gave product **3j** (79.7 mg, 0.184 mmol, 92%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 9.96 (s, 1H), 7.79-7.81 (m, 2H), 7.61-7.63 (m, 2H), 7.11-7.25 (m, 7H), 5.50 (s, 1H), 5.19 (s, 1H), 1.38 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 192.0 (s), 153.2 (s), 148.8 (s), 136.0 (s), 135.4 (s), 135.2 (s), 131.4 (s), 130.3 (s), 130.0 (s), 129.1 (s), 128.8 (s), 127.1 (s), 125.1 (s), 57.8 (s), 34.4 (s), 30.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{28}H_{33}O_2S$ $[M+H]^+$: 433.2201, found: 433.2200.

4-((4-Bromophenyl)(phenylthio)methyl)-2,6-di-tert-butylphenol (3k): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 40:1) gave product **3k** (89.7 mg, 0.186 mmol, 93%) as a colorless oil.[13a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.31-7.34 (m, 2H), 7.24-7.26 (m, 2H), 7.06-7.17 (m, 5H), 7.01 (s, 2H), 5.33 (s, 1H), 5.08 (s, 1H), 1.30 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.1 (s), 140.8 (s), 135.9 (s), 131.5 (s), 131.2 (s), 130.8 (s), 130.1 (s), 128.7 (s), 128.1 (s), 126.8 (s), 125.0 (s), 120.8 (s), 57.3 (s), 34.4 (s), 30.3 (s).

4-((2-Bromophenyl)(phenylthio)methyl)-2,6-di-tert-butylphenol (3l): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **3l** (92.6 mg, 0.192 mmol, 96%) as a colorless oil.[13a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.85-7.87 (m, 1H), 7.49-7.51 (m, 1H), 7.27-7.30 (m, 1H), 7.04-7.24 (m, 8H), 6.01 (s, 1H), 5.14 (s, 1H), 1.38 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.0 (s), 140.7 (s), 136.2 (s), 135.7 (s), 133.9 (s), 132.9 (s), 130.1 (s), 129.8 (s), 128.7 (s), 128.5 (s), 127.7 (s), 126.4 (s), 125.3 (s), 124.5 (s), 55.5 (s), 34.4 (s), 30.3 (s).

2,6-Di-tert-butyl-4-((4-fluorophenyl)(phenylthio)methyl)phenol (3m): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **3m** (75.2 mg, 0.178 mmol, 89%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.32-7.36 (m, 2H), 7.06-7.18 (m, 6H), 7.02 (s, 2H), 6.88-6.92 (m, 2H), 5.37 (s, 1H), 5.07 (s, 1H), 1.30 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 161.8 (d, ^{1}J(C,F) = 244.0 Hz), δ = 153.0 (s), 137.3 (d, ^{1}J(C,F) = 3.2 Hz), 136.0 (s), 135.8 (s), 131.2 (s), 131.1 (s), 129.9 (d, ^{1}J(C,F) = 8.0 Hz), 128.7 (s),

126.7 (s), 125.0 (s), 115.2 (d, ^1J(C,F) = 21.4 Hz), 57.2 (s), 34.4 (s), 30.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{27}H_{32}FOS$ $[M+H]^+$: 423.2158, found: 423.2153.

2,6-Di-tert-butyl-4-((3-fluorophenyl)(phenylthio)methyl)phenol (3n): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **3n** (71.8 mg, 0.17 mmol, 85%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.09-7.25 (m, 10H), 6.87-6.92 (m, 1H), 5.42 (s, 1H), 5.15 (s, 1H), 1.38 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 162.8 (d, ^1J(C,F) = 244.4 Hz), 153.1 (s), 144.3 (d, ^1J(C,F) = 6.6 Hz), 135.8 (s), 131.2 (s), 130.8 (s), 129.8 (d, ^1J(C,F) = 8.3 Hz), 128.7 (s), 126.8 (s), 125.0 (s), 124.4 (s), 124.1 (d, ^1J(C,F) = 2.9 Hz), 115.3 (d, ^1J(C,F) = 22.2 Hz), 114.0 (d, ^1J(C,F) = 21.1 Hz), 57.5 (s), 34.4 (s), 30.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{27}H_{32}FOS$ $[M+H]^+$: 423.2158, found: 423.2155.

4-((3,5-Di-tert-butyl-4-hydroxyphenyl)(phenylthio)methyl)benzonitrile (3o): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **3o** (78.1 mg, 0.182 mmol, 91%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.45-7.50 (m, 4H), 7.09-7.17 (m, 5H), 7.00 (s, 2H), 5.38 (s, 1H), 5.12 (s, 1H), 1.31 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.2 (s), 146.2 (s), 135.0 (s), 134.0 (s), 131.2 (s), 130.5 (s), 128.9 (s), 127.8 (s), 127.4 (s), 126.2 (s), 123.9 (s), 117.8 (s), 109.7 (s), 56.7 (s), 33.4 (s), 29.1 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{28}H_{32}NOS$ $[M+H]^+$: 430.2205, found: 430.2201.

2,6-Di-tert-butyl-4-((4-nitrophenyl)(phenylthio)methyl)phenol (3p): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **3p** (79.0 mg, 0.176 mmol, 88%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 8.22-8.23 (m, 1H), 7.97-8.00 (m, 1H), 7.71-7.73 (m, 1H), 7.35-7.39 (m, 1H), 7.14-7.17 (m, 2H), 7.09-7.12 (m, 3H), 7.04 (s, 2H), 5.44 (s, 1H), 5.13 (s, 1H), 1.31 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.4 (s), 148.2 (s), 144.1 (s), 136.2 (s), 134.9 (s), 134.5 (s), 131.9 (s), 130.0 (s), 129.3 (s), 128.9 (s), 127.4 (s), 125.0 (s), 123.5 (s), 122.1 (s), 57.5 (s), 34.4 (s), 30.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{27}H_{32}NO_3S$ $[M+H]^+$: 450.2103, found: 450.2100.

2,6-Dimethyl-4-(phenyl(phenylthio)methyl)phenol (3q): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 10:1) gave product **3q** (55.1 mg, 0.172 mmol,

86%) as a yellow oil. [13a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.40-7.42 (m, 2H), 7.24-7.30 (m, 2H), 7.09-7.22 (m, 6H), 7.01 (s, 2H), 5.43 (s, 1H), 4.57 (s, 1H), 2.18 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 151.4 (s), 141.5 (s), 136.6 (s), 132.5 (s), 130.1 (s), 128.6 (s), 128.5 (s), 127.1 (s), 126.3 (s), 123.1 (s), 56.8 (s), 16.1 (s).

2,6-Diisopropyl-4-(phenyl(phenylthio)methyl)phenol (3r): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 10:1) gave product **3r** (62.4 mg, 0.166 mmol, 83%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.42-7.44 (m, 2H), 7.27-7.30 (m, 2H), 7.09-7.24 (m, 6H), 7.04 (s, 2H), 5.48 (s, 1H), 4.72 (s, 1H), 3.03-3.13 (m, 2H), 1.19-1.21 (m, 12H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 149.1 (s), 141.5 (s), 136.4 (s), 133.5 (s), 132.7 (s), 130.9 (s), 128.6 (m), 128.4 (m), 128.3 (m), 127.0 (s), 126.5 (s), 123.7 (s), 57.6 (s), 27.3 (s), 22.7 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{25}H_{29}OS$ $[M+H]^+$: 377.1939, found: 377.1936.

2,6-Di-tert-butyl-4-((phenylthio)(pyridin-2-yl)methyl)phenol (3s): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 5:1) gave product **3s** (53.5 mg, 0.132 mmol, 66%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.56-8.57 (m, 1H), 7.58-7.65 (m, 2H), 7.23-7.24 (m, 2H), 7.12-7.18 (m, 6H), 5.59 (s, 1H), 5.14 (s, 1H), 1.37 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 160.9 (s), 153.2 (s), 149.3 (s), 136.7 (s), 135.8 (s), 131.2 (s), 130.2 (s), 128.7 (s), 126.7 (s), 125.3 (s), 122.7 (s), 122.0 (s), 59.3 (s), 34.4 (s), 30.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{26}H_{32}NOS$ $[M+H]^+$: 406.2205, found: 406.2202.

2,6-Di-tert-butyl-4-((phenylthio)(thiophen-3-yl)methyl)phenol (3t): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 5:1) gave product **3s** (64.0 mg, 0.156 mmol, 78%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.46-7.55 (m, 4H), 7.32-7.38 (m, 4H), 7.11 (s, 2H), 5.35 (s, 1H), 5.26 (s, 1H), 1.35 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 154.2 (s), 138.1 (s), 135.9 (s), 133.2 (s), 132.8 (s), 129.1 (s), 128.7 (s), 128.5 (s), 127.2 (s), 126.0 (s), 125.9 (s), 122.8 (s), 72.7 (s), 34.3 (s), 30.1 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{25}H_{31}OS_2$ $[M+H]^+$: 411.1816, found: 411.1812.

2,6-Di-tert-butyl-4-((2,3-dihydrobenzofuran-6-yl)(phenylthio)methyl)phenol (3u): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 30:1) gave product **3u**

(75.0 mg, 0.168 mmol, 84%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.29 (s, 1H), 7.11-7.23 (m, 8H), 6.70-6.71 (m, 1H), 5.41 (s, 1H), 5.12 (s, 1H), 4.55 (t, *J* = 8.7 Hz, 2H), 3.17 (*t*, J = 8.7 Hz, 2H), 1.39 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 159.1 (s), 152.8 (s), 136.7 (s), 135.6 (s), 133.7 (s), 131.9 (s), 131.0 (s), 128.6 (s), 128.1 (s), 127.2 (s), 126.4 (s), 125.1 (s), 124.9 (s), 108.9 (s), 71.4 (s), 57.6 (s), 34.4 (s), 30.3 (s), 29.8 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{29}H_{35}O_2S$ $[M+H]^+$: 447.2358, found: 447.2356.

2,6-Di-tert-butyl-4-(phenyl(p-tolylthio)methyl)phenol (4a): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4a** (71.1 mg, 0.17 mmol, 85%) as a colorless oil.[17a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.44-7.46 (m, 2H), 7.25-7.28 (m, 2H), 7.15-7.20 (m, 1H), 7.10-7.12 (m, 4H), 6.94-6.96 (m, 2H), 5.38 (s, 1H), 5.10 (s, 1H), 2.23 (s, 3H), 1.36 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.9 (s), 141.8 (s), 136.8 (s), 135.6 (s), 132.5 (s), 132.1 (s), 131.7 (s), 129.5 (s), 128.5 (s), 128.4(s), 127.0 (s), 125.2 (s), 58.6 (s), 34.4 (s), 30.3 (s), 21.2 (s).

2,6-Di-tert-butyl-4-(((4-methoxyphenyl)thio)(phenyl)methyl)phenol (4b): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4b** (69.5 mg, 0.16 mmol, 80%) as a colorless oil.[17a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.40-7.42 (m, 2H), 7.24-7.28 (m, 2H), 7.14-7.19 (m, 3H), 7.10 (s, 2H), 6.67-6.69 (m, 2H), 5.27 (s, 1H), 5.10 (s, 1H), 3.69 (s, 3H), 1.37 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 159.3 (s), 152.9 (s), 141.9 (s), 135.6 (s), 135.2 (s), 131.7 (s), 128.5 (s), 128.4 (s), 127.0 (s), 126.2 (s), 125.2 (s), 114.2 (s), 59.7 (s), 55.2 (s), 34.4 (s), 30.3 (s).

2,6-Di-tert-butyl-4-(((4-chlorophenyl)thio)(phenyl)methyl)phenol (4c): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4c** (79.9 mg, 0.182 mmol, 91%) as a colorless oil.[17a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.35-7.37 (m, 2H), 7.19-7.22 (m, 2H), 7.10-7.14 (m, 1H), 7.00-7.05 (m, 6H), 5.34 (s, 1H), 5.06 (s, 1H), 1.29 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.0 (s), 141.1 (s), 135.8 (s), 134.8 (s), 132.7 (s), 132.6 (s), 132.0 (s), 128.8 (s), 128.5 (s), 128.4 (s), 127.2 (s), 125.2 (s), 58.2 (s), 34.4 (s), 30.3 (s).

4-(((4-Bromophenyl)thio)(phenyl)methyl)-2,6-di-tert-butylphenol (4d): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4d** (82.9 mg, 0.172 mmol, 86%) as a colorless oil.[17a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.43-7.45 (m, 2H), 7.18-7.30 (m, 5H), 7.11 (s, 2H), 7.04-7.07 (m, 2H), 5.42 (s, 1H), 5.14 (s, 1H), 1.37 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.0 (s), 141.1 (s), 135.8 (s), 135.5 (s), 132.7 (s), 131.7 (s), 131.0 (s), 128.6 (s), 128.4 (s), 127.3 (s), 125.2 (s), 120.7 (s), 58.0 (s), 34.4 (s), 30.3 (s).

2,6-Di-tert-butyl-4-(((2-fluorophenyl)thio)(phenyl)methyl)phenol (4e): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4e** (74.3 mg, 0.176 mmol, 88%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.37-7.39 (m, 2H), 7.16-7.20 (m, 2H), 7.00-7.11 (m, 5H), 6.76-6.88 (m, 2H), 5.49 (s, 1H), 5.02 (s, 1H), 1.28 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 162.0 (d, ^1J(C,F) = 244.0 Hz), 153.0 (s), 141.1 (s), 135.6 (s), 134.3 (d, ^1J(C,F) = 1.7 Hz), 131.0 (s), 129.0 (d, ^1J(C,F) = 8.0 Hz), 128.4 (d, ^1J(C,F) = 3.8 Hz), 127.2 (s), 125.2 (s), 124.2 (d, ^1J(C,F) = 3.7 Hz), 122.9 (d, ^1J(C,F) = 17.8 Hz), 115.4 (d, ^1J(C,F) = 22.7 Hz), 56.9 (d, ^1J(C,F) = 2.3 Hz), 34.4 (s), 30.3 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{27}H_{32}FOS$ $[M+H]^+$: 423.2158, found: 423.2154.

2,6-Di-tert-butyl-4-(((2-fluorophenyl)thio)(phenyl)methyl)phenol (4f): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4f** (68.1 mg, 0.166 mmol, 83%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.34-7.36 (m, 2H), 7.20-7.23 (m, 2H), 7.14-7.17 (m, 2H), 7.05 (s, 2H), 6.74-6.77 (m, 2H), 5.21 (s, 1H), 5.01 (s, 1H), 1.31 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.1 (s), 141.1 (s), 135.7 (s), 134.9 (s), 133.9 (s), 130.8 (s), 130.0 (s), 128.6 (s), 128.4 (s), 127.2 (s), 127.1 (s), 125.2 (s), 61.7 (s), 34.4 (s), 30.3 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{25}H_{31}OS_2$ $[M+H]^+$: 411.1816, found: 411.1813.

2,6-Di-tert-butyl-4-((naphthalen-2-ylthio)(phenyl)methyl)phenol (4g): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4g** (78.0 mg, 0.172 mmol, 86%) as a colorless oil.[17a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.69-7.71 (m, 1H), 7.57-7.83 (m, 3H), 7.49-7.53 (m, 2H), 7.26-7.38 (m, 5H), 7.16-7.21 (m, 3H), 5.58 (s, 1H), 5.10 (s, 1H), 1.34 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 153.0 (s),141.5 (s), 135.8

(s), 133.8 (s), 133.6 (s), 132.0 (s), 131.4 (s), 129.7 (s), 128.9 (s), 128.5 (s), 128.4 (s), 128.1 (s), 127.6 (s), 127.3 (s), 127.2 (s), 126.3 (s), 125.9 (s), 125.3 (s), 57.9 (s), 34.4 (s), 30.3 (s).

4-((Benzylthio)(phenyl)methyl)-2,6-di-tert-butylphenol (4h): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4h** (76.1 mg, 0.182 mmol, 91%) as a colorless oil.[17a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.32-7.34 (m, 2H), 7.16-7.23 (m, 4H), 7.07-7.14 (m, 6H), 5.03 (s, 1H), 4.79 (s, 1H), 3.43 (s, 2H), 1.31 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.9 (s), 141.8 (s), 138.3 (s), 135.8 (s), 131.4 (s), 129.1 (s), 128.6 (s), 128.5 (s), 128.4 (s), 127.1 (s), 127.0 (s), 125.2 (s), 53.8 (s), 36.8 (s), 34.5 (s), 30.4 (s).

2,6-Di-tert-butyl-4-(((furan-2-ylmethyl)thio)(phenyl)methyl)phenol (4i): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4i** (61.5 mg, 0.15 mmol, 75%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.43-7.45 (m, 2H), 7.30-7.36 (m, 3H), 7.22-7.25 (m, 1H), 7.20 (s, 2H), 6.30 (s, 1H), 6.04 (s, 1H), 5.13 (s, 1H), 5.02 (s, 1H), 3.52 (s, 2H), 1.40 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.9 (s), 151.6 (s), 141.0 (s), 140.4 (s), 134.7 (s), 130.0 (s), 127.5 (s), 127.4(s), 126.0 (s), 124.0 (s), 109.3 (s), 106.4 (s), 52.9 (s), 33.3 (s), 29.2 (s), 27.7 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{26}H_{33}O_2S$ $[M+H]^+$: 409.2201, found: 409.2198.

2,6-Di-tert-butyl-4-(phenyl(propylthio)methyl)phenol (4j): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4j** (66.6 mg, 0.18 mmol, 88%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.44-7.46 (m, 2H), 7.30-7.34 (m, 2H), 7.19-7.24 (m, 3H), 5.12 (s, 1H), 4.98 (s, 1H), 1.96 (s, 3H), 1.40 (s, 18H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 152.8 (s), 141.48 (s), 135.7 (s), 131.7 (s), 128.5 (s), 128.4 (s), 127.0 (s), 124.9 (s), 56.4 (s), 34.4 (s), 30.3 (s), 16.0 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{22}H_{31}OS$ $[M+H]^+$: 343.2096, found: 343.2093.

2,6-Di-tert-butyl-4-(phenyl(propylthio)methyl)phenol (4k): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4k** (66.6 mg, 0.18 mmol, 90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 ^{o}C, TMS): δ = 7.36-7.38 (m, 2H), 7.20-7.24 (m, 2H), 7.10-7.14 (m, 3H), 5.03 (s, 1H), 4.99 (s, 1H), 2.20-2.31 (m, 2H), 1.45-1.50 (m, 2H), 1.32

(s, 18H), 0.84 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 152.8 (s), 142.4 (s), 135.7 (s), 132.0 (s), 128.5 (s), 128.4 (s), 126.9 (s), 124.9 (s), 54.5 (s), 34.5 (s), 34.4 (s), 30.4 (s), 22.5 (s), 13.7 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{24}H_{35}OS$ $[M+H]^+$: 371.2409, found: 371.2405.

2,6-Di-tert-butyl-4-((tert-butylthio)(phenyl)methyl)phenol (4l): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4l** (56.8 mg, 0.148 mmol, 74%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.48-7.50 (m, 2H), 7.25-7.29 (m, 2H), 7.14-7.21 (m, 3H), 5.13 (s, 1H), 5.08 (s, 1H), 1.40 (s, 18H), 1.22 (s, 9H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 152.6 (s), 144.1 (s), 135.7 (s), 133.4 (s), 128.4 (s), 128.3 (s), 126.7 (s), 125.0 (s), 52.7 (s), 44.5 (s), 34.5 (s), 31.4 (s), 30.4 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{25}H_{37}OS$ $[M+H]^+$: 385.2565, found: 385.2564.

3-((3,5-Di-tert-butyl-4-hydroxyphenyl)(phenyl)methyl)benzo[d]oxazole-2(3H)-thione (4m): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 20:1) gave product **4m** (82.1 mg, 0.178 mmol, 89%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.41 (s, 1H), 7.25-7.28 (m, 4H), 7.16-7.19 (m, 2H), 7.02-7.10 (m, 3H), 6.90-6.94 (m, 1H), 6.42-6.44 (m, 1H), 5.21 (s, 1H), 1.26 (s, 18H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 181.0 (s), 153.8 (s), 147.1 (s), 136.9 (s), 136.1 (s), 131.0 (s), 128.7 (s), 128.3 (s), 128.2 (s), 126.5 (s), 125.8 (s), 124.2 (s), 123.9 (s), 112.4 (s), 110.4 (s), 65.3 (s), 34.4 (s), 30.2 (s). HRMS (ESI) *m*/*z*: calcd. for $C_{28}H_{32}NO_2S$ $[M+H]^+$: 446.2154, found: 446.2151.

2,6-Di-tert-butyl-4-((tert-butylthio)(phenyl)methyl)phenol (6): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 5:1) gave product **6** (83.8 mg, 0.192 mmol, 96%) as a colorless oil.[17b] ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.60-7.63 (m, 2H), 7.55-7.57 (m, 2H), 7.47-7.51 (m, 1H), 7.30-7.36 (m, 5H), 7.19 (s, 2H), 5.25 (s, 1H), 5.20 (s, 1H), 1.35 (s, 18H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 154.2 (s), 138.5 (s), 135.9 (s), 133.4 (s), 133.2 (s), 130.0 (s), 129.1 (s), 128.7 (s), 128.5 (s), 128.4 (s), 127.1 (s), 123.2 (s), 76.8 (s), 34.3 (s), 30.2 (s).

2,6-Di-tert-butyl-4-(phenyl(phenylthio)methyl)phenol (3a'): According to the general procedure, work-up and flash column chromatography (*n*-hexane/EtOAc: 80:1) gave product **3a'** (76.8 mg, 0.19

mmol, 91%) as a yellow oil.[13a] ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 7.38-7.40 (m, 2H), 7.18-7.24 (m, 2H), 7.10-7.15 (m, 3H), 7.05-7.09 (m, 5H), 5.38 (s, 0.75 H), 5.04 (s, 1H), 1.30 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 151.8 (s), 140.5 (s), 135.3 (s), 134.6 (s), 130.3 (s), 130.1 (s), 127.5 (s), 127.4 (s), 127.3 (s), 126.0 (s), 125.5 (s), 124.1 (s), 56.9 (s), 33.4 (s), 29.2 (s).

Supporting Information Available: FAIR Data are available as Supporting Information for publication and includes the primary NMR FID files for compounds [**2s**-**2w**, **3a**-**3u**, **3a'**, **4a**-**4m**, **6**]. Copies of ^{1}H and $^{13}C\{^1H\}$ NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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References

(1) (a) Dunbar, K. L.; Scharf, D. H.; Litomska, A.; Hertweck, C. Enzymatic Carbon−Sulfur Bond Formation in Natural Product Biosynthesis. *Chem. Rev.* **2017**, *117*, 5521-5577. (b) Beletskaya, I. P.; Ananikov, V. P. Transition-Metal-Catalyzed C-S, C-Se, and C-Te Bond Formation via Cross-Coupling and Atom-Economic Addition Reactions. *Chem. Rev.* **2011**, *111*, 1596-1636. (c) Liu, B.; Lim, C.-H.; Miyake, G. M. Visible-Light-Promoted C-S Cross-Coupling via Intermolecular Charge Transfer. *J. Am. Chem. Soc.* **2017**, *139*, 13616-13619. (d) Zhang, G.; Liu, C.; Yi, H.; Meng, Q.; Bian, C.; Chen, H.; Jian, J.-X.; Wu, L.-Z.; Lei, A. External Oxidant-Free Oxidative Cross-Coupling: A Photoredox Cobalt-Catalyzed Aromatic C-H Thiolation for Constructing C-S Bonds. *J. Am. Chem. Soc.* **2015**, *137*, 9273-9280. (e) Oliver-Messeguer, J.; Liu, L.; García-García, S.; Canós-Giménez, C.; Domínguez, R.; Gavara, I.; Doménech-Carbó, A.; Concepción, P.; Leyva-Pérez, A.; Corma, A.; Stabilized Naked Sub-nanometric Cu Clusters within a Polymeric Film Catalyze C-N, C-C, C-O, C-S, and C-P Bond-Forming Reactions. *J. Am. Chem. Soc.* **2015**,

137, 3894-3900. (f) Sorribes, I.; Corma, A. Nanolayered cobalt-molybdenum sulphides (Co-Mo-S) catalyse borrowing hydrogen C-S bond formation reactions of thiols or H_2S with alcohols. *Chem. Sci.* **2019**, *10*, 3130-3142.

(2) Selected examples for the synthesis of diarylmethyl thioethers: (a) Jenkins, J. L.; Kao, R. Y. T.; Shapiro, R. Virtual Screening to Enrich Hit Lists From High Throughput Screening: A Case Study on Small-Molecule Inhibitors of Angiogenin. *Proteins*. **2003**, *50*, 81-93. (b) DeBonis, S.; Skoufias, D. A.; Indorato, R.-L.; Liger, F.; Marquet, B.; Laggner, C.; Joseph, B.; Kozielski, F. Structure-Activity Relationship of *S*-Trityl-L-Cysteine Analogues as Inhibitors of the Human Mitotic Kinesin Eg5. *J. Med. Chem.* **2008,** *51*, 1115-1125. (c) Toenjes, K. A.; Munsee, S. M.; Ibrahim, A. S.; Jeffrey, R.; Edwards, J. E.; Johnson, D. Small-Molecule Inhibitors of the Budded-to-Hyphal-Form Transition in the Pathogenic Yeast Candida albicansI. *Antimicrob. Agents Ch.* **2005**, *49*, 963-972. (d) Goyal, M.; Singh, P.; Alam, A.; Kumar Das, S.; Shameel Iqbal, M.; Dey, S.; Bindu, S.; Pal, C.; Kumar Das, S.; Panda, G.; Bandyopadhyay, U. Aryl aryl methyl thio arenes prevent multidrug-resistant malaria in mouse by promoting oxidative stress in parasites. *Free Radical Bio. Med.* **2012**, *53*, 129-142.

(3) Selected examples for the cross coupling of C-X bonds with R-S bonds: (a) Fernández-Rodríguez, M. A.; Shen, Q.; Hartwig, J. F. A General and Long-Lived Catalyst for the Palladium-Catalyzed Coupling of Aryl Halides with Thiols. *J. Am. Chem. Soc.* **2006**, *128*, 2180-2181. (b) Buchwald, S. L.; Bolm, C. On the Role of Metal Contaminants in Catalyses with $FeCl_3$. *Angew. Chem. Int. Ed.* **2009**, *48*, 5586-5587. (c) Bates, C. G.; Gujadhur, R. K.; Venkataraman, D. A General Method for the Formation of Aryl-Sulfur Bonds Using Copper(I) Catalysts. *Org. Lett.* **2002**, *4*, 2803-2806. (d) Li, G. Y.; Zheng, G.; Noonan, A. F. Highly Active, Air-Stable Versatile Palladium Catalysts for the C-C, C-N, and C-S Bond Formations via Cross-Coupling Reactions of Aryl Chlorides. *J. Org. Chem.* **2001**, *66*, 8677-8681. (e) Lv, X.; Bao, W. A *β*-Keto Ester as a Novel, Efficient, and Versatile Ligand for Copper(I)-Catalyzed C-N, C-O, and C-S Coupling Reactions. *J. Org. Chem.* **2007**, *72*, 3863-3867.

(4) Selected examples for the introduction of S-H bonds into an unsaturated carbon-carbon bonds: (a) Yang, D.; Yan, K.; Wei, W.; Zhao, J.; Zhang, M.; Sheng, X.; Li, G.; Lu, S.;Wang, H. Metal-Free Iodine-Catalyzed Direct Arylthiation of Substituted Anilines with Thiols. *J. Org. Chem.* **2015**, *80*, 6083-6092. (b) Cui, H.; Wei, W.; Yang, D.; Zhang, Y.; Zhao, H.; Wang, L.; Wang, H. Visible-light-induced selective synthesis of sulfoxides from alkenes and thiols using air as the oxidant. *Green Chem.* **2017**, *19*, 3520-3524. (c) Cui, H.; Liu, X.; Wei, W.; Yang, D.; He, C.; Zhang, T.; Wang, H. Molecular Iodine-Mediated Difunctionalization of Alkenes with Nitriles and Thiols Leading to β-Acetamido Sulfides. *J. Org. Chem.* **2016**, *81*, 2252-2260. (d) Yang, D.; Sun, P.; Wei, W.; Meng, L.; He, L.; Fang, B.; Jiang, W.; Wang, H. Metal-free iodine-catalyzed direct cross-dehydrogenative coupling (CDC) between pyrazoles and thiols. *Org. Chem. Front.* **2016**, *3*, 1457-1461. (e) Wang, L.; Yue, H.; Yang, D.; Cui, H.; Zhu, M.; Wang, J.; Wei, W.; Wang,

H. Metal-free Oxidative Coupling of Aromatic Alkenes with Thiols Leading to (*E*)-Vinyl Sulfones. *J. Org. Chem.* **2017**, *82*, 6857-6864.

(5) (a) Yang, C.; Gao, S.; Yao, H.; Lin, A. Rhodium-Catalyzed Hydroacylation of *para*-Quinone Methides with Salicylaldehydes: An Approach to α,α-Diaryl-2-Hydroxy Acetophenones. *J. Org. Chem.* **2016**, *81*, 11956-11964. (b) Yuan, Z.; Wei, W.; Lin, A.; Yao, H. Bifunctional Organo/Metal Cooperatively Catalyzed [3+2] Annulation of *para*-Quinone Methides with Vinylcyclopropanes: Approach to Spiro[4.5]deca-6,9-diene-8-ones. *Org. Lett.* **2016**, *18*, 3370-3373. (c) Li, X.; Xu, X.; Wei, W.; Lin, A.; Yao, H. Organocatalyzed Asymmetric 1,6-Conjugate Addition of *para*-Quinone Methides with Dicyanoolefins. *Org. Lett.* **2016**, *18*, 428-431. (d) Jarava-Barrera, C.; Parra, A.; López, A.; Cruz-Acosta, F.; Collado-Sanz, D.; Cárdenas, D. J.; Tortosa, M. Copper-Catalyzed Borylative Aromatization of *p*-Quinone Methides:Enantioselective Synthesis of Dibenzylic Boronates. *ACS Catal.* **2016**, *6*, 442-446. (e) Nigst, T. A.; Ammer, J.; Mayr, H. Ambident Reactivities of Methylhydrazines. *Angew. Chem. Int. Ed.* **2012**, *51*, 1353-1356. (f) Gai, K.; Fang, X.; Li, X.; Xu, J.; Wu, X.; Lin, A.; Yao, H. Synthesis of spiro[2.5]octa-4,7-dien-6-one with consecutive quaternary centers via 1,6-conjugate addition induced dearomatization of *para*-quinone methides. *Chem. Commun.* **2015**, *51*, 15831-15834. (g) Yuan, Z.; Pan, R.; Zhang, H.; Liu, L.; Lin, A.; Yao, H. Palladium-catalyzed Oxa-[4+2] Annulation of *para*-Quinone Methides *Adv. Synth. Catal.* **2017**, *359*, 4244-4249.

(6) (a) Yuan, Z.; Liu, L.; Pan, R.; Yao, H.; Lin, A. Silver-Catalyzed Cascade 1,6-Addition/Cyclization of *para*-Quinone Methides with Propargyl Malonates: An Approach to Spiro[4.5]deca-6,9-dien-8-ones. *J. Org. Chem.* **2017**, *82*, 8743-8751. (b) Yuan, Z.; Fang, X.; Li, X.; Wu, J.; Yao, H.; Lin, A. 1,6-Conjugated Addition-Mediated [2+1] Annulation: Approach to Spiro[2.5]octa-4,7-dien-6-one. *J. Org. Chem.* **2015**, *80*, 11123-11130. (c) Lin, C.; Shen, Y.; Huang, B.; Liu, Y.; Cui, S. Synthesis of Amides and Nitriles from Vinyl Azides and *p*-Quinone Methides. *J. Org. Chem.* **2017**, *82*, 3950-3956. (d) Wu, Q.-Y.; Ao, G.-Z.; Liu, F., Redox-neutral tri-/difluoromethylation of *para*-quinone methides with sodium sulfinates. *Org. Chem. Front.* **2018**, *5*, 2061-2064.

(7) (a) Ramanjaneyulu, B. T.; Mahesh, S.; Anand, R. V. Bis(amino)cyclopropenylidene-Catalyzed 1,6-Conjugate Addition of Aromatic Aldehydes to *para*-Quinone Methides: Expedient Access to α,α′-Diarylated Ketones. *Org. Lett.* **2015**, *17*, 3952-3955. (b) Arde, P.; Anand, R. V. Expedient access to unsymmetrical triarylmethanes through N-heterocyclic carbene catalysed 1,6-conjugate addition of 2-naphthols to *para*-quinone methides. *RSC Adv.* **2016**, *6*, 77111-77115. (c) He, F.-S.; Jin, J.-H.; Yang, Z.-T.; Yu, X.; Fossey, J. S.; Deng, W.-P. Direct Asymmetric Synthesis of β-Bis-Aryl-*α*-Amino Acid Esters via Enantioselective Copper-Catalyzed Addition of *p*-Quinone Methides *ACS Catal.* **2015**, *6*, 652-656. (d) Ma, C.; Huang, Y.; Zhao, Y. Stereoselective 1,6-Conjugate Addition/Annulation of *para*-Quinone Methides with Vinyl Epoxides/Cyclopropanes. *ACS Catal.* **2016**, *6*, 6408-6412. (e) Wang, J.; Rong, Q.; Zhao,

L.; Pan, X.; Zhao, L.; Zhao, K.; Hu, L.; Synthesis of 1,4-Dihydroquinolines and 4*H*-Chromenes via Organocatalytic Domino Aza/Oxa-Michael/1,6-Addition Reactions of *para*-Quinone Methides and Ynals. *J. Org. Chem.* **2020**, *85*, 11240-11249.

(8) (a) Mahesh, S.; Kant, G.; Anand, R. V. $B(C_6F_5)_3$ catalysed 1,6-conjugate allylation of *para*-quinone methides: expedient access to allyl diarylmethanes. *RSC Adv.* **2016**, *6*, 80718-80722. (b) Shen,Y.; Qi, J.; Mao, Z.; Cui, S. Fe-Catalyzed Hydroalkylation of Olefins with *para*-Quinone Methides. *Org. Lett.* **2016**, *18*, 2722-2725. (c) Huang, B.; Shen, Y.; Mao, Z.; Liu, Y.; Cui, S. Metathesis Reaction of Diazo Compounds and *para*-Quinone Methides for C-C Double Bond Formation: Synthesis of Tetrasubstituted Alkenes and Quinolinones. *Org. Lett.* **2016**, *18*, 4888-4891. (d) Zhao, K.; Zhi, Y.; Wang, A.; Enders, D. Asymmetric Organocatalytic Synthesis of 3-Diarylmethine Substituted Oxindoles Bearing a Quaternary Stereocenter via 1,6-Conjugate Addition to *para*-Quinone Methides. *ACS Catal.* **2016**, *6*, 657-660. (e) Ge, L.; Lu, X.; Cheng, C.; Chen, J.; Cao, W.; Wu, X.; Zhao, G. Amide-Phosphonium Salt as Bifunctional Phase Transfer Catalyst for Asymmetric 1,6-Addition of Malonate Esters to *para*-Quinone Methides. *J. Org. Chem.* **2016**, *81*, 9315-9325. (f) Xiong, B.; Wang, G.; Zhou, C.; Liu, Y.; Xu, W.; Xu, Y.-W.; Yang, C.-A.; Tang, K.-W. Base-Catalyzed Stereoselective 1,6-Conjugated Addition/Aromatization of P(O)–H Compounds with para-Quinone Methides. *Eur. J. Org. Chem.* **2019**, *2019*, 3273-3282.

(9) (a) Chu, W.-D.; Zhang, L.-F.; Bao, X.; Zhao, X.-H.; Zeng, C.; Du, J.-Y.; Zhang, G.-B.; Wang, F.-X.; Ma, X.-Y.; Fan, C.-A. Asymmetric Catalytic 1,6-Conjugate Addition/Aromatization of *para*-Quinone Methides: Enantioselective Introduction of Functionalized Diarylmethine Stereogenic Centers. *Angew. Chem. Int. Ed.* **2013**, *52*, 9229-9233. (b) Deng, Y.-H.; Zhang, X.-Z.; Yu, K.-Y.; Yan, X.; Du, J.-Y.; Huang, H.; Fan, C.-A. Bifunctional tertiary amine-squaramide catalyzed asymmetric catalytic 1,6-conjugate addition/aromatization of *para*-quinone methides with oxindoles. *Chem. Commun.* **2016**, *52*, 4183-4186. (c) Zhang, X.-Z.; Deng, Y.-H.; Yan, X.; Yu, K.-Y. Wang, F.-X.; Ma, X.-Y.; Fan, C.-A. Diastereoselective and Enantioselective Synthesis of Unsymmetric *β,β*-Diaryl-*α*-Amino Acid Esters via Organocatalytic 1,6-Conjugate Addition of *para*-Quinone Methides. *J. Org. Chem.* **2016**, *81*, 5655-5662.

(10) Caruana, L.; Kniep, F.; Johansen, T. K.; Poulsen; P. H.; Jørgensen, K. A. A New Organocatalytic Concept for Asymmetric *α*-Alkylation of Aldehydes. *J. Am. Chem. Soc.* **2014**, *136*, 15929-15932.

(11) Lou, Y.; Cao, P.; Jia, T.; Zhang, Y.; Wang, M.; Liao, J. Copper-Catalyzed Enantioselective 1,6-Boration of *para*-Quinone Methides and Efficient Transformation of gem-Diarylmethine Boronates to Triarylmethanes. *Angew. Chem. Int. Ed.* **2015**, *54*, 12134-12138.

(12) Dong, N.; Zhang, Z.-P.; Xue, X.-S.; Li, X.; Cheng, J.-P. Phosphoric Acid Catalyzed Asymmetric 1,6-Conjugate Addition of Thioacetic Acid to *para*-Quinone Methides. *Angew. Chem. Int. Ed.* **2016**, *55*, 1460-1464.

(13) (a) Jadhav, A. S.; Anand, R. V. Triflic Acid Catalyzed 1,6-Conjugate Addition of Thiols to *p*-Quinone Methides under Continuous-Flow Conditions. *Eur. J. Org. Chem.* **2017**, *25*, 3716-3721. (b) Liang, X.; Xu, H.; Li, H.; Chen, L.; Lu, H. Recyclable Bismuth Complex Catalyzed 1,6-Conjugate Addition of Various Nucleophiles to *para*-Quinone Methides: Expedient Access to Unsymmetrical Diaryl- and Triarylmethanes. *Eur. J. Org. Chem.* **2020**, *2*, 217-226.

(14) Selected examples for the generaiton of thiyl radicals: (a) Denes, F.; Pichowicz, M.; Povie, G.; Renaud, P. Thiyl Radicals in Organic Synthesis. *Chem. Rev.* **2014**, *114*, 2587-2693. (b) Oderinde, M. S.; Frenette, M.; Robbins, D. W.; Aquila, B.; Johannes, J. W. Photoredox Mediated Nickel Catalyzed Cross-Coupling of Thiols With Aryl and Heteroaryl Iodides via Thiyl Radicals. *J. Am. Chem. Soc.* **2016**, *138*, 1760-1763; (c) Chatgilialoglu, C.; Ferreri, C.; Guerra, M.; Samadi, A.; Bowry, V. W. The Reaction of Thiyl Radical with Methyl Linoleate: Completing the Picture. *J. Am. Chem. Soc.* **2017**, *139*, 4704-4714. (d) Wu, Z.; Chen, C.; Liu, J.; Lu, Y.; Xu, J.; Liu, X.; Cui, G.; Trabelsi, T.; Francisco, J. S.; Mardyukov, A.; Eckhardt, A. K.; Schreiner, P. R.; Zeng, X. Caged Nitric Oxide-Thiyl Radical Pairs. *J. Am. Chem. Soc.* **2019**, *141*, 3361-3365.

(15) Ma, X.; Yu, L.; Su, C.; Yang, Y.; Li, H.; Xu, Q. Efficient Generation of C-S Bonds via a By-Product-Promoted Selective Coupling of Alcohols, Organic Halides, and Thiourea. *Adv. Synth. Catal.* **2017**, *359*, 1649-1655.

(16) Lin, Y.-M.; Lu, G.-M.; Wang, G.-M.; Yi, W.-M. Acid/Phosphide-Induced Radical Route to Alkyl and Alkenyl Sulfides and Phosphonothioates from Sodium Arylsulfinates in Water. *J. Org. Chem.* **2017**, *82*, 382-389.

(17) (a) Liang, X.; Xu, H.; Li, H.; Chen, L.; Lu, H. Recyclable Bismuth Complex Catalyzed 1,6-Conjugate Addition of Various Nucleophiles to *para*-Quinone Methides: Expedient Access to Unsymmetrical Diaryl- and Triarylmethanes. *Eur. J. Org. Chem.* **2020**, *2*, 217-226. (b) Liu, Z.-Q.; You, P.-S.; Zhang, L.-D.; Liu, D.-Q.; Liu, S.-S.; Guan, X.-Y. TBAB-Catalyzed 1,6-Conjugate Sulfonylation of *para*-Quinone Methides: A Highly Efficient Approach to Unsymmetrical gem-Diarylmethyl Sulfones in Water. *Molecules.* **2020**, *25*, 539-553.

(18) CCDC-2010097 (**4m**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.