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Cu-Mediated Sulfonyl Radical-Enabled 5-*exo*-*trig* Cyclization of Alkenyl Aldehydes: Access to Sulfonylmethyl 1*H*-Indenes

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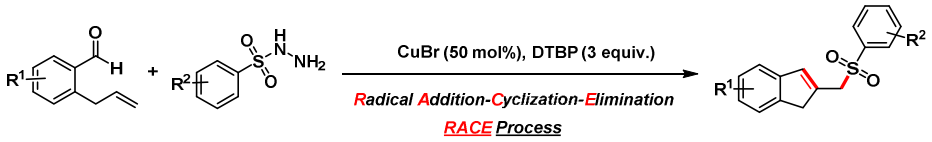


ABSTRACT: An efficient method for the construction of sulfonylmethyl 1*H*-indenes via Cu(I)-mediated sulfonyl radical-enabled 5-*exo*-*trig* cyclization of alkenyl aldehydes has been developed for the first time. Mechanistic studies indicated that a radical addition-cyclization-elimination (*RACE*) process might be involved. The reaction features relatively broad substrate scope, good annulation efficiency and various functional group tolerance.

INTRODUCTION

Indene derivatives are important cyclic compounds that serve as building blocks for natural products[1] and pharmaceutical compounds[2] possessing interesting biological activities, as well as many functional materials[3] (Figure 1). They can also be used as valuable ligands for indenyl metal complexes, which are widely utilized in various catalytic reactions[4]. Due to their importance and usefulness, various synthetic approaches have been developed to construct indene derivatives including intramolecular[5] and intermolecular[6] cyclization reactions. In spite of this progress, there is still a need to develop new methods that can expand the structural scope with wide functionality and use inexpensive catalysts through simple synthetic manipulations.

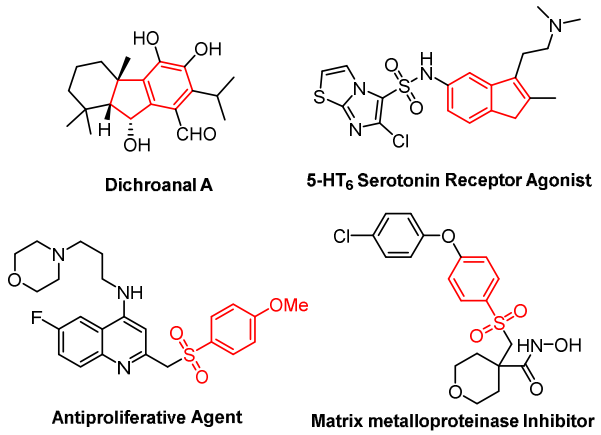
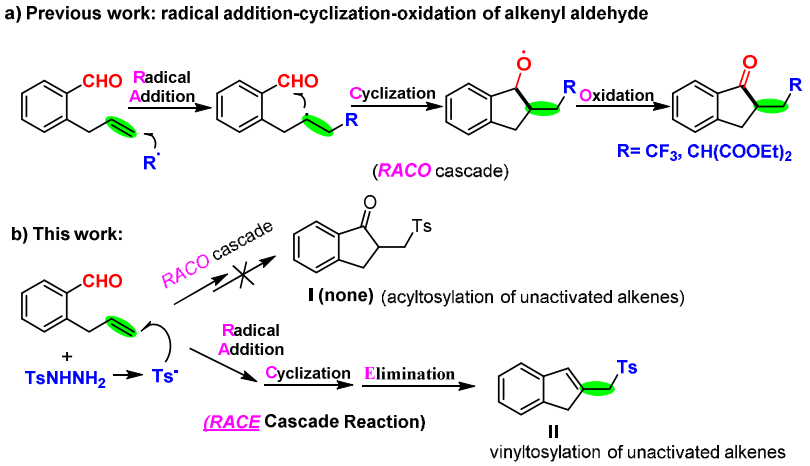


Figure 1. Selected examples of important indenes and sulfones

Meanwhile, sulfonyl-containing compounds are of great importance in functional transformation of many pharmaceuticals, agrochemicals and materials[7], especially for aryl alkyl sulfones[8] (Figure 1), however, available methods to easily accessing alkyl sulfone are limited.[9]

Recently, Zhu and coworkers[10] developed a tandem radical addition-cyclization-oxidation (RACO) reaction process to realize acylalkylation of inactivated alkenes. In this strategy, formation of a nucleophilic carbon radical favors the intramolecular addition to aldehydes, and subsequent oxidation facilitated a series of substituted indanones (Scheme 1a).

Scheme 1. Radical initiated cascade reaction of alkenyl aldehydes.

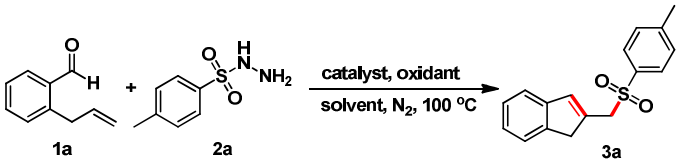


By taking advantage of the powerful radical chemistry[11] and in view of the success in using a sulfonyl radical to attack C-C unsaturated bonds to achieve sulfones,[12,13] we envisioned that using a sulfonyl radical other than the alkyl carbon radicals in Zhu's work would convert the same alkenyl substrates to acylsulfonylated products **I** (sulfonylmethyl indenones, Scheme 1b) through a similar RACO cascade process. Surprisingly, treatment of sulfonyl hydrazide, the sulfonyl radical precursor,[12c] with 2-allylbenzaldehyde under CuBr/DTBP catalyst/oxidant system[14] did not generate the desired **I**, instead, an eliminated product **II** (sulfonylmethyl indene) was obtained as the major product. Herein, we reported optimization of the reaction condition, exploration of the substrate scope and limitation as well the discussion of the possible reaction mechanism (RACE cascade reaction).

RESULTS AND DISCUSSION

Initially, we commenced the reaction with 2-allyl benzaldehyde (**1a**) and *p*-toluenesulfonyl hydrazide (**2a**) as model substrates (Table 1). To our delight, product **3a** was obtained in 30% yield with CuI as the catalyst, di-*tert*-butyl peroxide (DTBP) as the oxidant and acetonitrile as the solvent (entry 1). Then effects of copper salts were investigated, which elected CuBr as the most efficient catalyst, giving **3a** in 51% yield (entries 2-7). Next, an array of different oxidants, such as *tert*-butyl hydroperoxide (TBHP), *tert*-butyl peroxybenzoate (TBPB) and dicumyl peroxide (DCP), were examined and the results were no better than the case of DTBP (entries 2, 8-10). In addition, employment of other solvents such as toluene, DMSO, DMF and 1,4-dioxane provided inferior results (entries 11-14). Further, increasing the loading of CuBr to 50 mol% slightly promoted the yield (entry 17). From these results, the optimum reaction condition was determined as those in entry 17.

Table 1. Optimization of Reaction Conditions[a]



1a 2a 3a

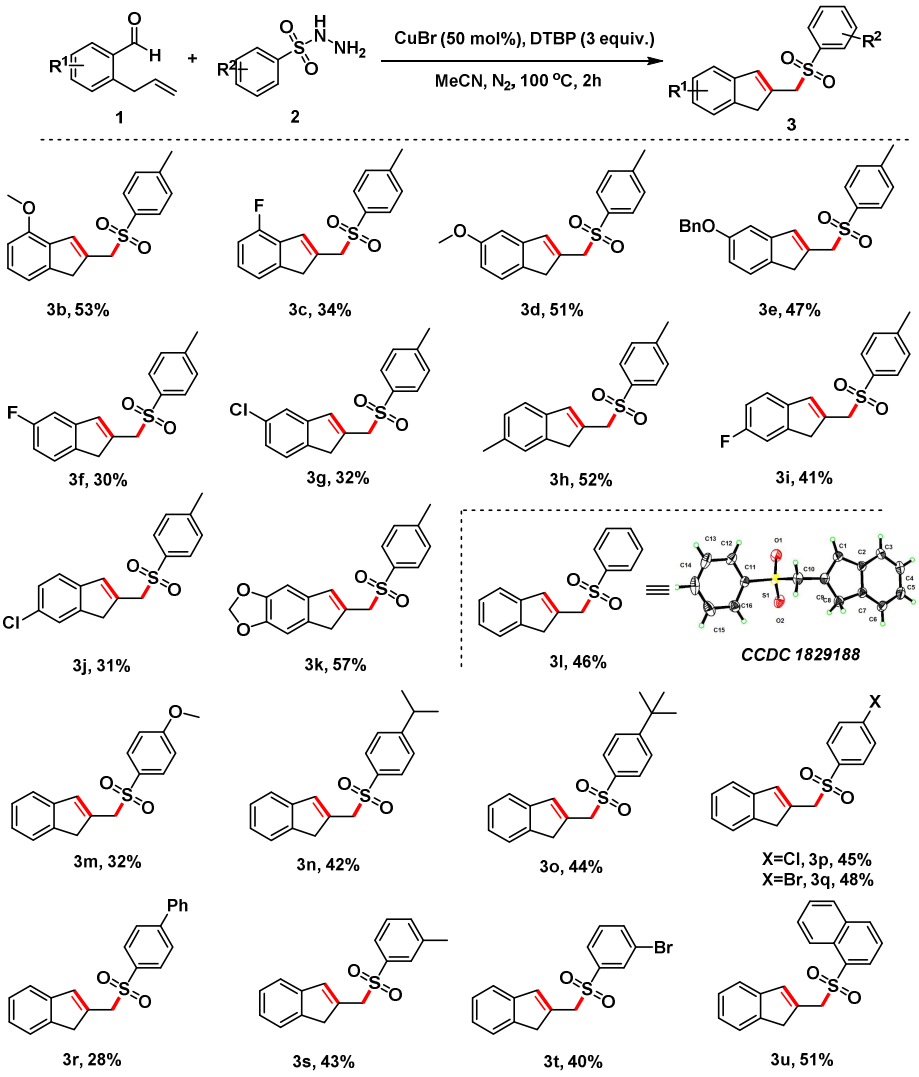
entry	Catalyst (mol%)	oxidant	solvent	yield[%][b]
1	CuI (20)	DTBP	MeCN	30
2	CuBr (20)	DTBP	MeCN	51
3	CuCl (20)	DTBP	MeCN	17
4	CuOAc (20)	DTBP	MeCN	6
5	$Cu(MeCN)_4PF_6$ (20)	DTBP	MeCN	11
6	$CuSO_4$ (20)	DTBP	MeCN	13
7	$Cu(OAc)_2$ (20)	DTBP	MeCN	Trace
8	CuBr (20)	TBHP[c]	MeCN	30
9	CuBr (20)	TBPB	MeCN	39
10	CuBr (20)	DCP	MeCN	25
11	CuBr (20)	DTBP	PhMe	20
12	CuBr (20)	DTBP	DMSO	21
13	CuBr (20)	DTBP	DMF	13
14	CuBr (20)	DTBP	1,4-dioxane	17
15	CuBr (30)	DTBP	MeCN	50
16	CuBr (40)	DTBP	MeCN	48
17	***CuBr (50)***	***DTBP***	***MeCN***	**56 (57[d,e])**
18	CuBr (60)	DTBP	MeCN	52

[a]Reactions were carried out by using 1a (0.10 mmol), 2a (0.20 mmol), Catalyst, Oxidant (0.30 mmol), solvent (0.5 ml), 100 °C, N_2, 2h. [b]The yield was determined by ^1H NMR using CH_2Br_2 as the internal standard. [c]TBHP (5.5 M in nonane). [d]Isolated yield. [e]1.0 mmol scale. DTBP: Di-*tert*-butyl peroxide. TBHP: *tert*-Butyl hydroperoxide. TBPB: *tert*-Butyl peroxybenzoate. DCP: Dicumyl peroxide.

With the optimized reaction conditions in hand, we evaluated its versatility and limitation in the Cu(I)-mediated sulfonyl radical-enabled 5-*exo*-*trig* cyclization of various alkenyl aldehydes. As illustrated in Scheme 2, all the reactions went through smoothly and the sulfonated products **3** were obtained in moderate

yields. The *ortho*-substituted aldehydes **1b** and **1c** were converted into the corresponding products **3b** and **3c** in 53% and 34% yield, respectively, implying that the electronic property rather than steric hindrance of the substituent near the aldehyde group has more impact on the reaction. Substrates **1d-k** bearing the electron-donating groups such as MeO-, BnO-, and Me-, or electron-withdrawing groups such as F-, and Cl-, showed good compatibility, and the corresponding products **3d−k** were obtained in 30−57% yields. In general, substrates having electron-donating substituents went through at higher reactivity, indicating that the electronic effect of the aldehyde group in substrates has a significant correlation with the reaction efficiency.

Scheme 2. Substrates Scope for Synthesis of 3[a,b]



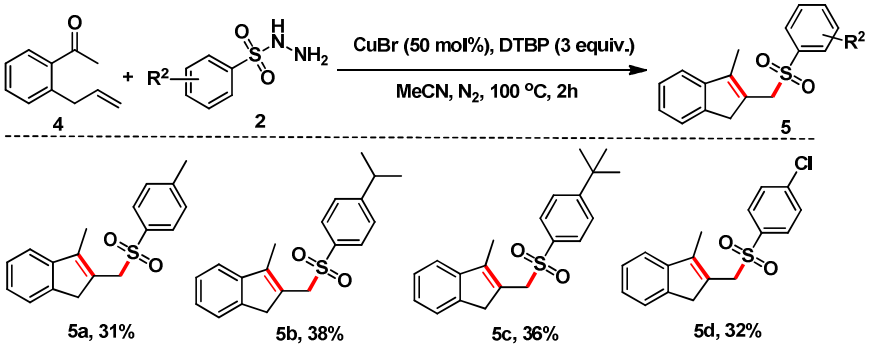
[a]Reactions were carried out by using **1** (0.1 mmol), **2** (0.2 mmol), CuBr (0.05 mmol, 50 mol %), DTBP (0.6 mmol), MeCN (0.5 mL), 100 °C, N_2, 2 h. [b]Isolated yield.

In the meantime, sulfonyl hydrazides bearing different substituents were examined as well. Benzenesulfonhydrazide and derivatives with MeO-, ^{i}Pr-, and ^{t}Bu- substituents at the *para*-position went through the reaction smoothly and gave desired products **3l-3o** in 32-46% yields. Halide substituents, such as Cl and Br, tolerated the standard reaction conditions, thus providing possible access for further functional

transformations (**3p-q**). However, the yield dropped to 28 % in the case of sulfonyl hydrazide bearing a bulky biphenyl group (**3r**).[15] Sulfonyl hydrazides with substituents such as Me- or Br-, at the *meta*-position also reacted smoothly with substrate **1a** and provided corresponding products **3s-t** in moderate yields. In addition, naphthalene-1-sulfonohydrazide also showed good reactivity, giving product **3u** in 51% yield.

More appealingly, the scope of this reaction was not restricted to alkenyl aldehydes as the substrates. Indeed, 1-(2-allylphenyl)ethan-1-one **4** was found also suitable for this cascade reaction (Scheme 3), thus providing disubstituted indenes **5a-d**, although the yields were relatively lower (31-38%).

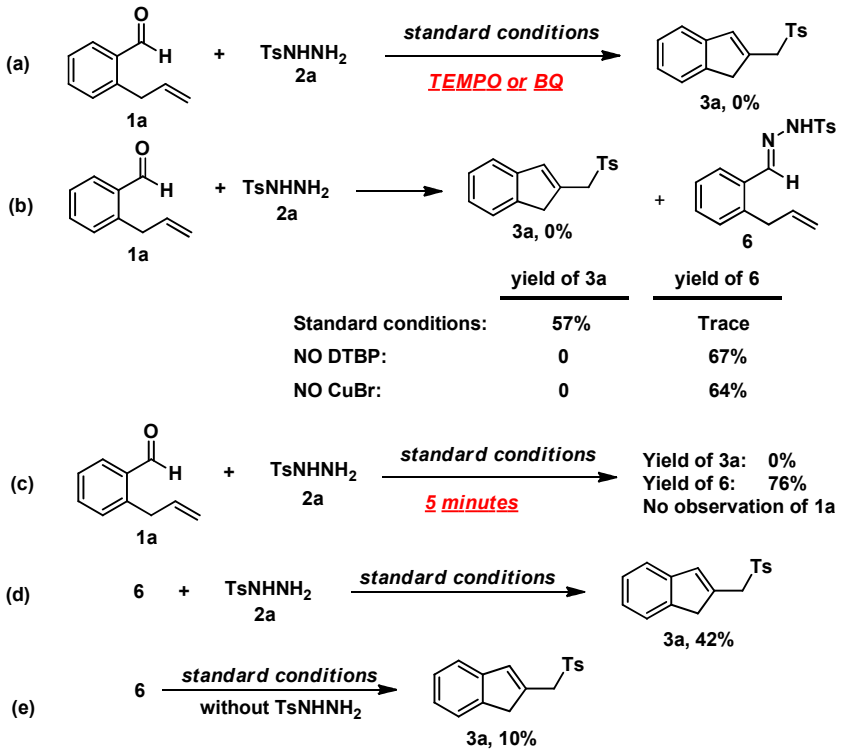
Scheme 3. Substrates Scope for Synthesis 5[a,b]



[a]Reactions were carried out by using **4** (0.1 mmol), **2** (0.2 mmol), CuBr (0.05 mmol, 50 mol %), DTBP (0.6 mmol), MeCN (0.5 mL), 100 °C, N_2, 2 h. [b]Isolated yield.

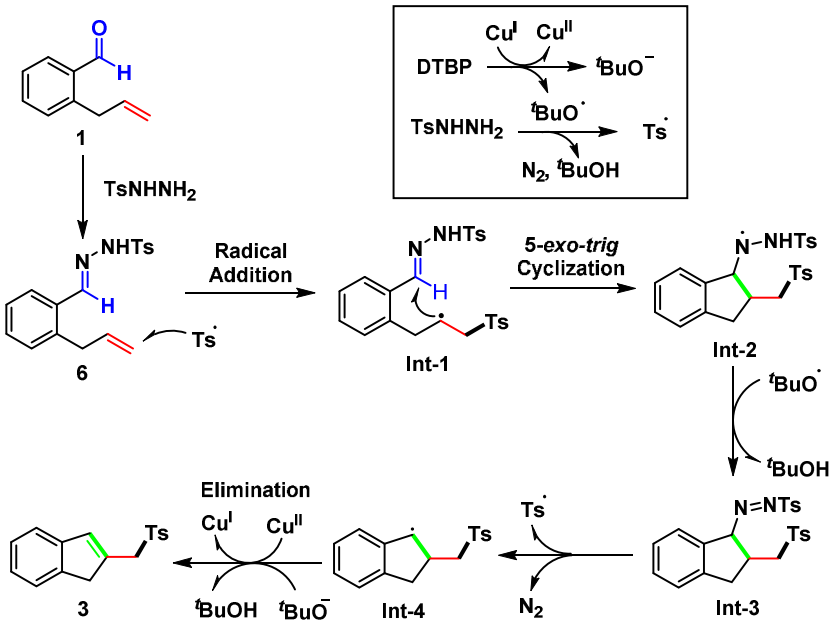
To gain some insights into the reaction mechanism, a series of control experiments were performed (Scheme 4). First, radical scavenger experiments were implemented. We found that radical scavengers, such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 1,4-benzoquinone (BQ), significantly suppressed the reaction progress, confirming that the proposed radical process is indeed involved (Scheme 4a). During optimization of reaction conditions, we found that the reaction failed to proceed without either DTBP or CuBr, and the major byproduct sulfonohydrazone **6** could be isolated in 64-67% yield (Scheme 4b). This result suggested that the copper salt and the oxidant DTBP are indispensable for the reaction; otherwise, the reaction process would stop at the formation of sulfonohydrazone **6**. To provide further support for the reaction pathway, we stopped the reaction at an early stage and found **1a** could be completely transformed to **6** (Scheme 4c). Subsequent treatment of **6** with **2a** under standard conditions gave the desired product **3a** in 42% yield (Scheme 4d), suggesting that the reaction might involve the *in situ* formation of sulfonohydrazone **6**. Sulfonohydrazone **6** was found to proceed alone the cascade reaction very sluggishly under the standard conditions without addition of **2a**, leading to **3a** in 10% yield (Scheme 4e), indicating the Ts radical to attack the terminal vinyl carbon was primarily from another equivalent of **2a**, not from the intermediate **6**.

Scheme 4. Mechanistic Studies



Based on the experiments above and the literature reports,[10,13f,14] a proposed mechanism for the current Cu(I)-mediated sulfonyl radical-enabled cyclization of alkenyl aldehydes is proposed. As shown in Scheme 5, the first step involves formation of sulfonohydrazone **6** from 2-allyl benzaldehyde **1** and sulfonyl hydrazide **2**. In the meantime, sulfonyl radical is formed *in situ* from the oxidative decomposition of sulfonyl hydrazide **2** mediated by copper salt and DTBP[14], which then attacks the terminal vinyl carbon of substrate **1** to give the nucleophilic alkyl radical **Int-1**. Subsequent intramolecular 5-*exo*-*trig* cyclization and H-abstraction give the intermediate **Int-3**, which is then converted to the radical species **Int-4** by releasing the sulfonyl radical and N_2.[13f] Finally, indene **3** is formed from the intermediate **Int-4** through a copper (II)-mediated single electron transfer oxidation to generate a carbocation species, which then undergoes elimination process via β-H-abstraction by $^{t}BuO^{-}$.[16] It should be mentioned that the overall moderate yield of the reaction is likely due to the high reactivity of the alkenyl aldehyde substrates and the incomplete conversion of the sulfonohydrazone intermediates.

Scheme 5. Proposed Reaction Mechanism



In conclusion, we have reported a novel and efficient approach to prepare 2-sulfonylmethyl 1*H*-indene derivatives via Cu(I)-mediated sulfonyl radical-enabled 5-*exo-trig* cyclization strategy. The transformation possesses a relatively broad substrate scope with good functional group compatibility, thus leading to vinylsulfonylation of inactivated alkenes to yield various sulfonylmethyl indenes. Mechanism study indicates that the reaction may occur through a tandem cascade process involving radical addition-cyclization-elimination process (RACE).

EXPERIMENTAL SECTION

General Information. All reactions were performed in flame-dried glassware using sealed tubes or Schleck tubes. Liquids and solutions were transferred with syringes. All solvents and chemical reagents were obtained from commercial sources and used without further purification. ^{1}H and ^{13}C NMR spectra were recorded with tetramethylsilane as an internal reference. Low- and high-resolution mass spectra were recorded on EI-TOF (electrospray ionization/time-of-flight). Flash column chromatography on silica gel (200−300 mesh) was used for the routine purification of reaction products. The column output was monitored by TLC on silica gel (100−200 mesh) precoated on glass plates (15 × 50 mm), and spots were visualized by UV light at 254 nM. General procedure for the preparation of starting materials 1 and 4 was according to the literature procedures.[10,17] Starting materials arylsulfonyl hydrazides were prepared according to the literature procedures.[18]

General Procedure for Synthesis of Sulfonylmethyl 1*H*-Indenes. *Example for the Synthesis of **3a**.* To an oven-dried 10 mL sealed tube was added substrate **1a** (14.6 mg, 0.10 mmol), 4-methylbenzenesulfonohydrazide **2a** (37.2 mg, 0.20 mmol), CuBr (7.2 mg, 0.050 mmol), DTBP (55 μL, 0.30 mmol) and acetonitrile (0.5 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography (eluent: PE/DCM = 2/3), to afford the desired product **3a**.

2-(Tosylmethyl)-1*H*-indene (**3a**). White solid, yield: 57 % (16.2 mg); mp 173-174 °C. ^{1}H NMR (300

MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 7.0 Hz, 1H), 7.31 – 7.26 (m, 3H), 7.25 – 7.16 (m, 2H), 6.58 (s, 1H), 4.25 (s, 2H), 3.51 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 144.0, 143.7, 135.4, 135.2, 134.3, 129.7, 128.4, 126.4, 125.3, 123.7, 121.2, 59.0, 41.5, 21.6; Ms (EI): *m/z* = 284 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{17}H_{16}O_2S$, 284.0866; Found, 284.0874.

4-Methoxy-2-(tosylmethyl)-1*H*-indene (**3b**). White solid, yield: 53 % (16.8 mg); mp 90-91 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.20 – 7.13 (m, 1H), 7.04 (d, J = 7.5 Hz, 1H), 6.78 – 6.72 (m, 2H), 4.23 (s, 2H), 3.82 (s, 3H), 3.53 (s, 2H), 2.42 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.1, 146.0, 144.7, 135.5, 132.5, 132.2, 131.6, 129.7, 128.3, 126.7, 116.6, 108.4, 59.1, 55.4, 41.8, 21.6; Ms (EI): *m/z* = 314 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{18}H_{18}O_3S$, 314.0971; Found, 314.0970.

4-Fluoro-2-(tosylmethyl)-1*H*-indene (**3c**). White solid, yield: 34 % (10.3 mg); mp 135-136 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.23 – 7.13 (m, 2H), 6.94 (t, J = 8.7 Hz, 1H), 6.66 (s, 1H), 4.24 (s, 2H), 3.61 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.1 (d, J = 249.4 Hz), 147.0 (d, J = 5.5 Hz), 144.9, 135.3, 134.5, 130.8 (d, J = 16.3 Hz), 129.8, 129.7, 128.3, 126.9 (d, J = 6.7 Hz), 119.6 (d, J = 3.2 Hz), 113.0 (d, J = 19.6 Hz), 58.9, 41.9, 21.6; Ms (EI): *m/z* = 302 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{17}H_{15}FO_2S$, 302.0771; Found, 302.0769.

5-Methoxy-2-(tosylmethyl)-1*H*-indene (**3d**). White solid, yield: 51 % (16.0 mg); mp 144-145 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.32 – 7.25 (m, 3H), 6.84 (d, J = 2.3 Hz, 1H), 6.76 (dd, J = 8.2, 2.4 Hz, 1H), 6.53 (s, 1H), 4.23 (s, 2H), 3.80 (s, 3H), 3.43 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.8, 145.0, 144.7, 136.1, 135.7, 135.4, 135.1, 129.7, 128.4, 124.1, 111.4, 106.7, 59.0, 55.4, 40.8, 21.6; Ms (EI): *m/z* = 314 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{18}H_{18}O_3S$, 314.0971; Found, 314.0969.

5-(Benzyloxy)-2-(tosylmethyl)-1*H*-indene (**3e**). White solid, yield: 47 % (18.2 mg); mp 143-144 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 2H), 7.46 – 7.31 (m, 5H), 7.31 – 7.26 (m, 3H), 6.91 (d, J = 2.2 Hz, 1H), 6.83 (dd, J = 8.2, 2.4 Hz, 1H), 6.52 (s, 1H), 5.06 (s, 2H), 4.22 (s, 2H), 3.43 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.1, 145.0, 144.7, 137.2, 136.4, 135.7, 135.4, 135.1, 129.7, 128.5, 128.4, 127.9, 127.4, 124.1, 112.3, 107.8, 70.3, 59.0, 40.8, 21.6; Ms (EI): *m/z* = 390 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{24}H_{22}O_3S$, 390.1284; Found, 390.1294.

5-Fluoro-2-(tosylmethyl)-1*H*-indene (**3f**). White solid, yield: 30 % (9.0 mg); mp 175-176 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.36 – 7.27 (m, 3H), 7.00 – 6.83 (m, 2H), 6.53 (s, 1H), 4.23 (s, 2H), 3.49 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.2 (d, J = 242.7 Hz), 145.3 (d, J = 9.3 Hz), 144.9, 139.2 (d, J = 2.1 Hz), 136.8, 135.4, 134.5 (d, J = 3.1 Hz), 129.8, 128.4, 124.4 (d, J = 9.1 Hz), 112.1 (d, J = 23.1 Hz), 108.2 (d, J = 23.2 Hz), 58.9, 40.9, 21.6; Ms (EI): *m/z* = 302 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{17}H_{15}FO_2S$, 302.0771; Found, 302.0767.

5-Chloro-2-(tosylmethyl)-1*H*-indene (**3g**). White solid, yield: 32 % (10.2 mg); mp 192-193 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.1 Hz, 2H), 7.35 – 7.29 (m, 3H), 7.26 (s, 1H), 7.17 (d, J = 8.0 Hz, 1H), 6.50 (s, 1H), 4.23 (s, 2H), 3.51 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 144.9, 142.1, 136.5, 135.3, 134.2, 132.4, 129.8, 128.4, 125.3, 124.6, 121.4, 58.9, 41.1, 21.6; Ms (EI): *m/z* = 318 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{17}H_{15}ClO_2S$, 318.0476; Found, 318.0470.

6-Methyl-2-(tosylmethyl)-1*H*-indene (**3h**). White solid, yield: 52 % (15.6 mg); mp 151-152 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.24 (s, 1H), 7.17 (d, J = 7.7 Hz, 1H), 7.06 (d, J = 7.7 Hz, 1H), 6.52 (s, 1H), 4.23 (s, 2H), 3.47 (s, 2H), 2.43 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.7, 144.3, 141.1, 135.4, 135.1, 135.0, 133.2, 129.6, 128.4, 127.2, 124.6, 120.8, 59.0, 41.2, 21.6, 21.5; Ms (EI): *m/z* = 298 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{18}H_{18}O_2S$, 298.1022; Found, 298.1023.

6-Fluoro-2-(tosylmethyl)-1*H*-indene (**3i**). White solid, yield: 41 % (12.4 mg); mp 174-175 °C. ^{1}H NMR

(300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.20 (dd, J = 8.3, 5.1 Hz, 1H), 7.12 (d, J = 8.7 Hz, 1H), 6.99 – 6.90 (m, 1H), 6.55 (s, 1H), 4.21 (s, 2H), 3.50 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 161.6 (d, J = 244.4 Hz), 146.0 (d, J = 8.8 Hz), 144.8, 139.7 (d, J = 2.0 Hz), 135.5, 134.4, 133.9 (d, J = 3.9 Hz), 129.7, 128.3, 121.8 (d, J = 8.8 Hz), 113.5 (d, J = 23.1 Hz), 111.4 (d, J = 23.4 Hz), 58.8, 41.6 (d, J = 2.0 Hz), 21.6; Ms (EI): m/z = 302 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{17}H_{15}FO_2S$, 302.0771; Found, 302.0772.

6-Chloro-2-(tosylmethyl)-1*H*-indene (**3j**). White solid, yield: 31 % (10.0 mg); mp 193-194 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, J = 8.3 Hz, 2H), 7.39 (s, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.23 – 7.17 (m, 2H), 6.56 (s, 1H), 4.22 (s, 2H), 3.50 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 144.9, 142.2, 135.4, 134.8, 134.4, 131.5, 129.8, 128.3, 126.7, 124.1, 121.9, 58.8, 41.4, 21.6; Ms (EI): m/z = 318 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{17}H_{15}ClO_2S$, 318.0476; Found, 318.0480.

6-(Tosylmethyl)-5*H*-indeno[5,6-*d*][1,3]dioxole (**3k**). White solid, yield: 57 % (18.8 mg); mp 177-178 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (t, J = 6.7 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 6.91 (s, 1H), 6.76 (s, 1H), 6.46 (s, 1H), 5.95 (s, 2H), 4.19 (s, 2H), 3.41 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 146.3, 144.7, 138.0, 137.4, 135.5, 134.8, 132.8, 129.6, 128.4, 105.1, 102.0, 100.9, 59.0, 41.3, 21.6; Ms (EI): m/z = 328 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{18}H_{16}O_4S$, 328.0764; Found, 328.0774.

2-((Phenylsulfonyl)methyl)-1*H*-indene (**3l**). White solid, yield: 46 % (13.2 mg); mp 137-138 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 – 7.77 (m, 2H), 7.64 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.6 Hz, 2H), 7.42 (d, J = 6.8 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.25 – 7.17 (m, 2H), 6.56 (s, 1H), 4.27 (s, 2H), 3.52 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 143.7, 138.3, 135.3, 134.1, 133.8, 129.1, 128.4, 126.5, 125.4, 123.7, 121.3, 58.9, 41.5; Ms (EI): m/z = 270 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{16}H_{14}O_2S$, 270.0709; Found, 270.0703.

2-(((4-Methoxyphenyl)sulfonyl)methyl)-1*H*-indene (**3m**). White solid, yield: 32 % (10.0 mg); mp 123-124 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 2H), 7.42 (d, J = 7.7 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.26 – 7.15 (m, 2H), 6.98 – 6.91 (m, 2H), 6.57 (s, 1H), 4.24 (s, 2H), 3.86 (s, 3H), 3.51 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 144.0, 143.7, 135.1, 134.6, 130.6, 129.9, 126.4, 125.3, 123.7, 121.2, 114.2, 59.1, 55.6, 41.5; Ms (EI): m/z = 300 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{17}H_{16}O_3S$, 300.0815; Found, 300.0818.

2-(((4-Isopropylphenyl)sulfonyl)methyl)-1*H*-indene (**3n**). White solid, yield: 42 % (13.8 mg); mp 110-111 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2H), 7.42 (d, J = 6.9 Hz, 1H), 7.35 (d, J = 8.4 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.25 – 7.16 (m, 2H), 6.60 (s, 1H), 4.25 (s, 2H), 3.51 (s, 2H), 2.98 (hept, J = 6.9 Hz, 1H), 1.26 (d, J = 6.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5, 144.0, 143.8, 135.8, 135.2, 134.3, 128.5, 127.2, 126.4, 125.3, 123.7, 121.2, 59.0, 41.5, 34.2, 23.6; Ms (EI): m/z = 312 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{19}H_{20}O_2S$, 312.1179; Found, 312.1176.

2-(((4-(*tert*-Butyl)phenyl)sulfonyl)methyl)-1*H*-indene (**3o**). White solid, yield: 44 % (14.8 mg); mp 156-157 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 7.0 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.26 – 7.16 (m, 2H), 6.61 (s, 1H), 4.25 (s, 2H), 3.51 (s, 2H), 1.33 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.7, 144.0, 143.8, 135.5, 135.2, 134.3, 128.2, 126.4, 126.1, 125.3, 123.6, 121.2, 59.0, 41.5, 35.2, 31.0; Ms (EI): m/z = 326 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{20}H_{22}O_2S$, 326.1335; Found, 326.1332.

2-(((4-Chlorophenyl)sulfonyl)methyl)-1*H*-indene (**3p**). White solid, yield: 45 % (14.2 mg); mp 131-132 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 7.1 Hz, 2H), 7.51 – 7.41 (m, 3H), 7.32 – 7.28 (m, 1H), 7.26 – 7.17 (m, 2H), 6.57 (s, 1H), 4.26 (s, 2H), 3.54 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 143.5, 140.6, 136.7, 135.6, 133.8, 129.9, 129.4, 126.5, 125.5, 123.7, 121.4, 59.0, 41.5; Ms (EI): m/z = 304 $[M]^+$; HRMS (EI): m/z $[M]^+$ Calcd for $C_{16}H_{13}ClO_2S$, 304.0319; Found, 304.0323.

2-(((4-Bromophenyl)sulfonyl)methyl)-1*H*-indene (**3q**). White solid, yield: 48 % (17.3 mg); mp 139-140

°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (s, 4H), 7.44 (d, J = 6.9 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.27 – 7.18 (m, 2H), 6.58 (s, 1H), 4.26 (s, 2H), 3.54 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 143.5, 137.3, 135.6, 133.7, 132.4, 129.9, 129.2, 126.5, 125.5, 123.7, 121.4, 58.9, 41.5; Ms (EI): *m/z* = 348 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{16}H_{13}BrO_2S$, 347.9814; Found, 347.9811.

2-(([1,1'-Biphenyl]-4-ylsulfonyl)methyl)-1*H*-indene (**3r**). White solid, yield: 28 % (10 mg); mp 219-220 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.83 (m, 2H), 7.75 – 7.68 (m, 2H), 7.64 – 7.58 (m, 2H), 7.53 – 7.41 (m, 4H), 7.32 – 7.18 (m, 3H), 6.63 (s, 1H), 4.31 (s, 2H), 3.56 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.7, 144.0, 143.7, 139.0, 136.9, 135.4, 134.2, 129.1, 128.9, 128.7, 127.6, 127.4, 126.5, 125.4, 123.7, 121.3, 59.0, 41.5; Ms (EI): *m/z* = 346 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{22}H_{18}O_2S$, 346.1022; Found, 346.1026.

2-((*m*-Tolylsulfonyl)methyl)-1*H*-indene (**3s**). White solid, yield: 43 % (12.9 mg); mp 121-122 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 – 7.55 (m, 2H), 7.45 – 7.34 (m, 3H), 7.31 – 7.27 (m, 1H), 7.26 – 7.15 (m, 2H), 6.60 (s, 1H), 4.25 (s, 2H), 3.51 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 143.7, 139.4, 138.2, 135.3, 134.5, 134.1, 128.9, 128.6, 126.4, 125.5, 125.3, 123.6, 121.2, 58.9, 41.5, 21.2; Ms (EI): *m/z* = 284 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{17}H_{16}O_2S$, 284.0866; Found, 284.0863.

2-(((3-Bromophenyl)sulfonyl)methyl)-1*H*-indene (**3t**). White solid, yield: 40 % (14.7 mg); mp 154-155 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.79 – 7.74 (m, 1H), 7.71 (dd, J = 7.9, 0.6 Hz, 1H), 7.44 (d, J = 6.9 Hz, 1H), 7.37 (t, J = 7.9 Hz, 1H), 7.33 – 7.28 (m, 1H), 7.27 – 7.19 (m, 2H), 6.62 (s, 1H), 4.27 (s, 2H), 3.55 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 143.5, 140.2, 136.9, 135.8, 133.5, 131.2, 130.5, 127.1, 126.5, 125.5, 123.7, 123.2, 121.4, 58.9, 41.5; Ms (EI): *m/z* = 348 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{16}H_{13}BrO_2S$, 347.9814; Found, 347.9805.

1-(((1*H*-inden-2-yl)methyl)sulfonyl)naphthalene (**3u**). White solid, yield: 51 % (17 mg); mp 148-149 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 8.6 Hz, 1H), 8.15 (dd, J = 7.4, 1.2 Hz, 1H), 8.11 (d, J = 8.3 Hz, 1H), 7.99 (d, J = 8.1 Hz, 1H), 7.72 (ddd, J = 8.5, 7.0, 1.5 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.52 – 7.46 (m, 1H), 7.37 (d, J = 6.3 Hz, 1H), 7.22 – 7.13 (m, 3H), 6.43 (s, 1H), 4.47 (s, 2H), 3.46 (s, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.9, 143.7, 135.3, 135.2, 134.1, 134.0, 133.5, 131.2, 129.3, 129.0, 128.8, 127.0, 126.4, 125.3, 124.3, 124.0, 123.6, 121.2, 58.3, 41.5; Ms (EI): *m/z* = 320 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{20}H_{16}O_2S$, 320.0866; Found, 320.0862.

3-Methyl-2-(tosylmethyl)-1*H*-indene (**5a**). White solid, yield: 31 % (9.3 mg); mp 133-134 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 7.3 Hz, 1H), 7.32 – 7.20 (m, 5H), 4.23 (s, 2H), 3.52 (s, 2H), 2.43 (s, 3H), 1.61 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.3, 144.7, 143.2, 141.5, 135.6, 129.7, 128.4, 127.2, 126.2, 125.5, 123.5, 119.3, 57.0, 41.1, 21.6, 10.0; Ms (EI): *m/z* = 298 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{18}H_{18}O_2S$, 298.1022; Found, 298.1008.

2-(((4-Isopropylphenyl)sulfonyl)methyl)-3-methyl-1*H*-indene (**5b**). White solid, yield: 38 % (12.4 mg); mp 105-106 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 6.5 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.25 – 7.19 (m, 2H), 4.22 (s, 2H), 3.52 (s, 2H), 2.97 (hept, J = 6.9 Hz, 1H), 1.58 (t, J = 2.0 Hz, 3H), 1.25 (d, J = 6.9 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.5, 145.3, 143.2, 141.5, 135.7, 128.6, 127.3, 127.2, 126.2, 125.5, 123.5, 119.3, 57.0, 41.1, 34.2, 23.6, 9.9; Ms (EI): *m/z* = 326 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{20}H_{22}O_2S$, 326.1335; Found, 326.1327.

2-(((4-(*tert*-Butyl)phenyl)sulfonyl)methyl)-3-methyl-1*H*-indene (**5c**). White solid, yield: 36 % (12.2 mg); mp 142-143 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.64 (m, 2H), 7.51 – 7.45 (m, 2H), 7.43 (d, J = 6.6 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.25 – 7.20 (m, 2H), 4.22 (s, 2H), 3.53 (s, 2H), 1.57 (t, J = 2.1 Hz, 3H), 1.33 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.8, 145.3, 143.2, 141.5, 135.4, 128.3, 127.3, 126.2, 126.1, 125.5, 123.5, 119.3, 57.0, 41.1, 35.2, 31.0, 9.9; Ms (EI): *m/z* = 340 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{21}H_{24}O_2S$, 340.1492; Found, 340.1496.

2-(((4-Chlorophenyl)sulfonyl)methyl)-3-methyl-1*H*-indene (**5d**). White solid, yield: 32 % (10.2 mg); mp 125-126 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 – 7.67 (m, 2H), 7.49 – 7.42 (m, 3H), 7.34 – 7.28 (m, 1H), 7.26 – 7.21 (m, 2H), 4.25 (s, 2H), 3.54 (s, 2H), 1.64 (t, J = 2.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.1, 143.1, 141.9, 140.6, 137.0, 129.9, 129.4, 126.6, 126.4, 125.7, 123.5, 119.5, 57.0, 41.1, 10.2; Ms (EI): *m/z* = 318 $[M]^+$; HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{17}H_{15}ClO_2S$, 318.0476; Found, 318.0480.

1 mmol-scale synthesis of 3a. To an oven-dried 25 mL sealed tube was added substrate **1a** (146.2 mg, 1.0 mmol), 4-methylbenzenesulfonohydrazide **2a** (372.4 mg, 2.0 mmol), CuBr (71.7 mg, 0.50 mmol), DTBP (551 μL, 3.0 mmol) and acetonitrile (2.0 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent: PE/EA = 5/1), to afford 161.2 mg (57%) of the desired product **3a.**

Radical Trapping Experiments (Scheme 4a). To an oven-dried 10 mL sealed tube was added substrate **1a** (14.6 mg, 0.10 mmol), 4-methylbenzenesulfonohydrazide **2a** (37.2 mg, 0.20 mmol), CuBr (7.2 mg, 0.050 mmol), TEMPO (46.9 mg, 3.0 equiv) or 1,4-benzoquinone (32.4 mg, 3.0 equiv), DTBP (55 μL, 0.30 mmol) and acetonitrile (0.5 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The yield of product **3a** was based on ^{1}H NMR analysis of the crude product.

Control Experiment 1 (Scheme 4b). To an oven-dried 10 mL sealed tube was added *o*-allylbenzaldehyde tosylhydrazone **6** (31.4 mg, 0.10 mmol), 4-methylbenzenesulfonohydrazide **2a** (37.2 mg, 0.20 mmol), CuBr (7.2 mg, 0.050 mmol) and acetonitrile (0.5 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography (eluent: PE/DCM = 2/3), to afford the *o*-allylbenzaldehyde tosylhydrazone **6** (21 mg, 67 %). Thus the reactions were repeated in the absence of CuBr, affording 20 mg of the *o*-allylbenzaldehyde tosylhydrazone **6** in 64% yield.

Control Experiment 2 (Scheme 4c). To an oven-dried 10 mL sealed tube was added **1a** (14.6 mg, 0.10 mmol), 4-methylbenzenesulfonohydrazide **2a** (37.2 mg, 0.20 mmol), CuBr (7.2 mg, 0.050 mmol), DTBP (55 μL, 0.30 mmol) and acetonitrile (0.5 mL) under a nitrogen atmosphere. The mixture was stirred for 5 min at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography (eluent: PE/DCM = 2/3), to afford the *o*-allylbenzaldehyde tosylhydrazone **6** (23.9 mg, 76 %).

Control Experiment 3 (Scheme 4d). To an oven-dried 10 mL sealed tube was added *o*-allylbenzaldehyde tosylhydrazone **6** (31.4 mg, 0.10 mmol), 4-methylbenzenesulfonohydrazide **2a** (37.2 mg, 0.20 mmol), CuBr (7.2 mg, 0.050 mmol), DTBP (55 μL, 0.30 mmol) and acetonitrile (0.5 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography (eluent: PE/DCM = 2/3), to afford the desired product **3a** (12 mg, 42 %).

Control Experiment 4 (Scheme 4c). To an oven-dried 10 mL sealed tube was added *o*-allylbenzaldehyde tosylhydrazone **6** (31.4 mg, 0.10 mmol), CuBr (7.2 mg, 0.050 mmol), DTBP (55 μL, 0.30 mmol) and acetonitrile (0.5 mL) under a nitrogen atmosphere. The mixture was stirred for 2 h at 100 °C. The mixture was then cooled to room temperature, diluted with DCM, filtered through a celite pad, and concentrated in vacuo. The residue was purified by preparative thin-layer chromatography (eluent: PE/DCM = 2/3), to afford the desired product **3a** (2.9 mg, 10 %).

ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra for new compounds and X-ray crystallography data for compound **3l**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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