Synthesis Y. Zhao et al. Special Topic

Metal-Free [3+2] Oxidative Coupling of Phenols with Alkenes: Synthesis of Dihydrobenzofurans

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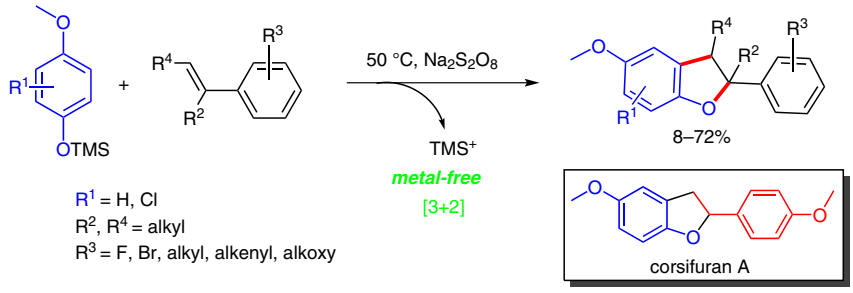


Received: 11.03.2015
Accepted after revision: 14.04.2015
Published online: 27.05.2015
DOI: 10.1055/s-0034-1380419; Art ID: ss-2015-c0155-st

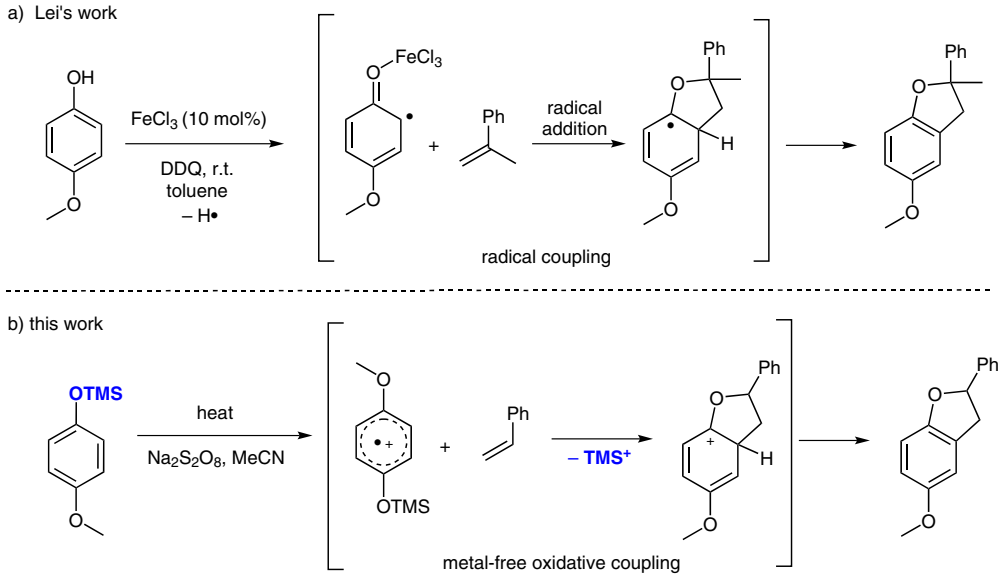
Abstract Herein, we demonstrated a benign and metal-free [3+2]-cycloaddition reaction using simple and readily available phenols and styrenes as substrates and sodium persulfate as an inexpensive and environmentally friendly oxidant for the direct synthesis of dihydrobenzofurans. This methodology was applied to the synthesis of corsifuran A in a single step.

Key words metal-free, phenols, alkenes, sodium persulfate, dihydrobenzofuran

Hydrobenzofurans have attracted the attention of many chemists by virtue of their potential biological and pharmacological activity and structural diversity; the 2,3-dihydrobenzofuran skeleton represents the core of many interesting bioactive compounds,[1] such as 3′,4-di-*O*-methylcedrusin,[2] (+)-conocarpan,[3] and corsifuran A.[4] There are numerous reports of their synthesis in the literature and new synthetic methods have also been extensively investigated,[5] of which inter- and intramolecular cyclization reactions play a vital role. Previous examples of the synthesis of dihydrobenzofurans have generally focused on the application of transition-metal catalysis,[6] organic acids,[7] and electrochemical methods[8] to enable cycloaddition of phenols/quinones to olefins/alkynes or other complex synthetic substrates; their limitations are that the conditions are not economic or the product is accompanied by a number of byproducts. Therefore, the development of a benign and practical avenue to access dihydrobenzofurans remains of interest.[9]

Phenols are largely commercially available chemicals and they are readily oxidized in the presence of a variety of oxidants. Over the past few decades, oxidative phenol coupling has been applied to the formation of dimeric products and the biosynthesis of natural products.[10] Recently, Lei and co-workers[11] reported an iron(III) chloride catalyzed radical cross-coupling of alkenes with phenols for the construction of the dihydrobenzofuran moiety [Scheme 1 (a)]. Based upon our continued work on radical chemistry,[12] we found that phenols could undergo single-electron transfer and generate a putative phenoxyl cation by oxidative quenching of the photoredox catalytic conditions, and this is then trapped by styrene to form dihydrobenzofurans with little to no side products. Coincidentally, similar work was recently reported by the group of T. P. Yoon[13] while our manuscript was in preparation. However, our investigations showed that such an oxidative [3+2]-cycloaddition reaction could also be achieved in the absence of photoredox catalysis using trimethylsilyl-protected phenols by heating [Scheme 1 (b)].

It is well precedented that persulfate ($S_2O_8^{2-}$) decomposes on heating or by light irradiation to form the sulfate radical[14] which is a strong oxidant. Thus our initial investigation was carried out on 4-methoxyphenol and styrene (**2a**) (4 equiv) in the presence of sodium persulfate (3 equiv) in acetonitrile at 50 °C. To our delight, the desired cycloaddition product **3aa** was obtained in 28% yield after 48 hours. When trimethylsilyl-protected 4-methoxyphenol **1a** was used, the yield improved to 34% under similar reaction conditions (Table 1, entry 3). Other protective groups, such as acetyl led to low yields or no reaction. Therefore, (4-methoxyphenoxy)trimethylsilane (**1a**) and styrene (**2a**) were used as model substrates to optimize the reaction conditions (Table 1). A brief screening of other oxidants, such as ammonium persulfate and potassium persulfate, indicated that sodium persulfate was the ideal oxidant (entries 1 and 2). An examination of the reaction temperature showed that 50 °C was the optimal choice when compared with room temperature or higher temperatures (70 °C) (entries 4–6). It is noteworthy that a higher temperature could pro-

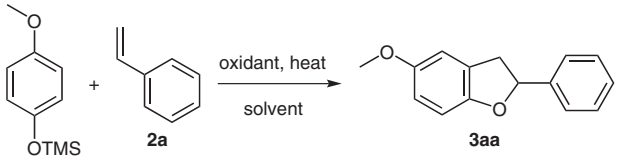


Scheme 1 Reported synthesis of dihydrobenzofuran and our strategy

mote the consumption of starting material, yet more complicated byproducts were formed. Further optimization of the reaction conditions examined the solvent, which has a significant effect on the reaction efficiency. No reaction of the starting material was observed by TLC when the reaction was performed in *N*,*N*-dimethylformamide, methanol, tetrahydrofuran, and dichloromethane (entries 7–10). Further examination of the amount of oxidant led to the desired product **3aa** in lower yields (entries 11 and 12). Finally, the optimal reaction conditions, (4-methoxyphenoxy)trimethylsilane (**1a**) (1 equiv) and styrene (**2a**) (4 equiv) in acetonitrile with heating to 50 °C in the presence of sodium persulfate (3 equiv), gave the desired product **3aa** in 72% isolated yield (entry 5).

With the optimized conditions in hand, we next examined the scope of the reaction using various alkenes bearing either electron-donating or electron-withdrawing groups on aromatic rings. As shown in Scheme 2, terminal alkenes substituted with *para*- or *ortho*-electron-donating groups, such as methyl and *tert*-butyl, reacted smoothly with **1a** to afford the corresponding products **3ab**, **3ac**, and **3ad** in good yields. However, 4- and 3-methoxystyrene produced the expected products **3af** and **3ag** in moderate yields together with byproducts from the oxidation of styrene containing a methoxy group by sodium persulfate. Halogen groups (Br and F) were also tolerated well in this protocol to afford the 2,3-dihydrobenzofurans **3ah** and **3ai**, respectively. Moreover, we tested steric effects of α- and β-substituted styrenes. To our delight, **3ak** and **3al** containing a quaternary center were readily prepared from α-methyl- and α-cyclopropylstyrenes in 61% and 70% yield, respectively. In addition, styrenes with β-substitution were also competent substrates and produced the corresponding cycloadducts **3am**, **3an**, and **3ao** in moderate yields. Indene also reacted with **1a** successfully to give the desired product **3aj**. Nota-

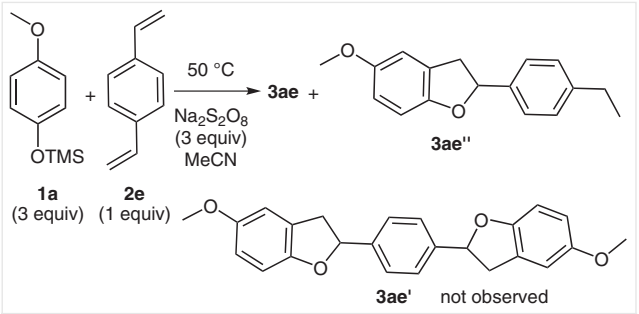
Table 1 Optimization of the Reaction Conditions



Entry[a]	Oxidant	Temp (°C)	Solvent	Yield[b] (%)
1[c]	$(NH_4)_2S_2O_8$	50	MeCN	14
2[c]	$K_2S_2O_8$	50	MeCN	9
3[c]	$Na_2S_2O_8$	50	MeCN	34
4	$Na_2S_2O_8$	r.t. (~30)	MeCN	9
5	$Na_2S_2O_8$	50	MeCN	82 (72[d])
6	$Na_2S_2O_8$	70	MeCN	50
7	$Na_2S_2O_8$	50	DMF	0
8	$Na_2S_2O_8$	50	MeOH	0
9	$Na_2S_2O_8$	50	THF	0
10	$Na_2S_2O_8$	50	CH_2Cl_2	0
11	$Na_2S_2O_8$ (2 equiv)	50	MeCN	27
12	$Na_2S_2O_8$ (4 equiv)	50	MeCN	49

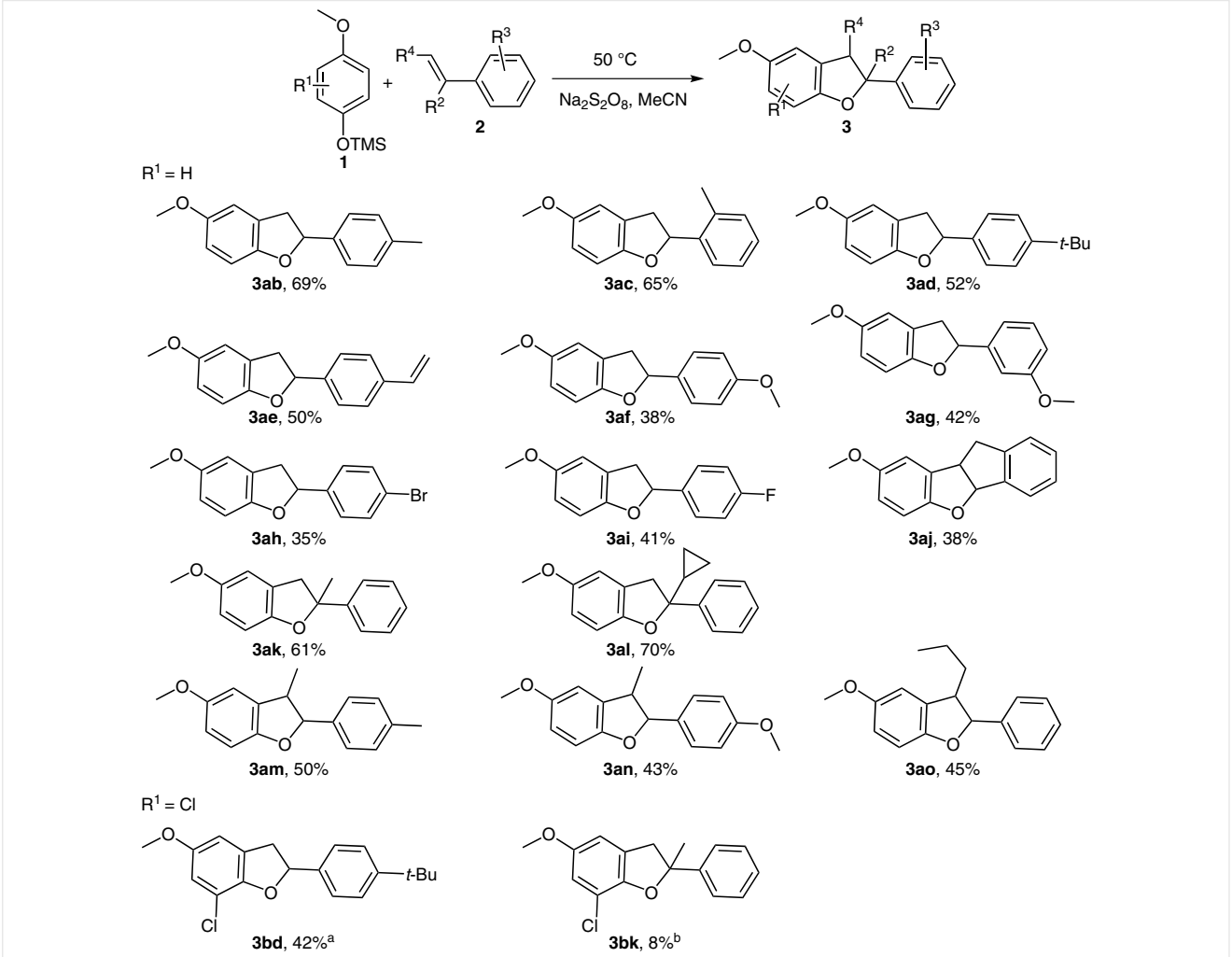
[a] Reaction conditions: **1a** (0.15 mmol), **2a** (0.6 mmol), oxidant (3 equiv), solvent (0.1 M), 70 h, unless otherwise stated.
[b] Yield determined by GC-MS.
[c] Reacted for 48 h.
[d] Isolated yield.

bly, the monocycloadduct **3ae** was obtained in moderate yield when 1.5 equivalents of 1,4-divinylbenzene reacted under the optimal reaction conditions. We, therefore, envisioned that modifying the reaction conditions by decreasing of the amount of 1,4-divinylbenzene (**2e**) to one equivalent and increasing the amount of **1a** to three equivalents could potentially give benzodifuran **3ae′** in one step (Equation 1). However, the reaction provided a mixture of **3ae** and **3ae″** with a reduced C=C double bond. In addition, 4-methoxyphenols containing halogen groups, such as the chloride **1b** (R^1 = Cl), were prepared and found to be suitable substrates giving the corresponding cycloadducts **3bd** and **3bk**, which may have potential applications by further functionalization, albeit the starting materials **1** and **2** were recovered after reacting for 72 hours.



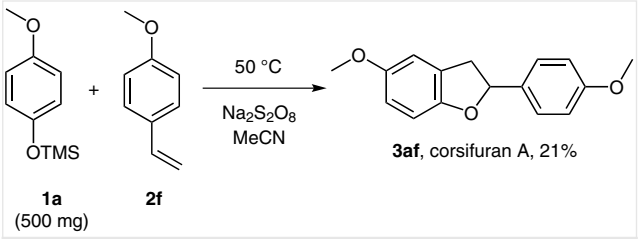
Equation 1 Reaction of **1a** with **2e**

To test the application of this protocol in organic synthesis, we carried out a scaled up experiment to prepare the natural product corsifuran A (**3af**). When **1a** (500 mg)



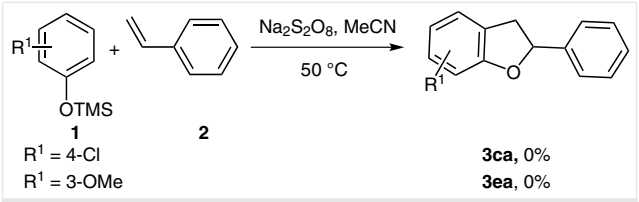
Scheme 2 Substrate scope of the metal-free [3+2] cycloaddition. *Reagents and conditions*: **1** (0.15 mmol), **2** (0.6 mmol), $Na_2S_2O_8$ (0.45 mmol), MeCN (0.1 M), except in the case of **3ae**: alkene **2e** (0.3 mmol). Yields were based on the isolated products (after reaction, substrates **1** remain in most cases). [a] 2-Chloro-4-methoxyphenol (25%) was recovered. [b] 2-Chloro-4-methoxyphenol (49%) was recovered.

reacted under the standard conditions, corsifuran A (**3af**) was obtained in 21% yield after 72 hours (Equation 2).



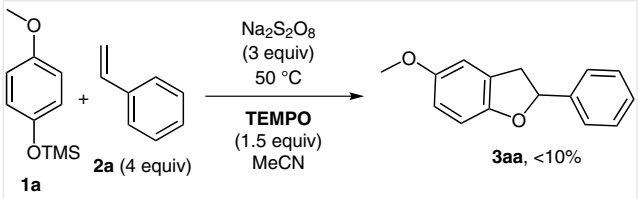
Equation 2 One-step synthesis of corsifuran A

Additionally, a number of styrenes with electron-withdrawing groups in the β-position were also examined under the optimal reaction conditions, but the reactions failed to give the desired cycloaddition products (see the Supporting Information). We also examined the oxidative [3+2] cyclization of styrene with other phenol derivatives, such as 4-chlorophenol and 3-methoxyphenol, but they failed to give the corresponding products (Scheme 3). The experimental results presented show that electron-rich phenols bearing 4-methoxy were necessary for successful cycloaddition (more examples, see the Supporting Information). This observation is consistent with the report by Lei[11] and Yoon.[13]



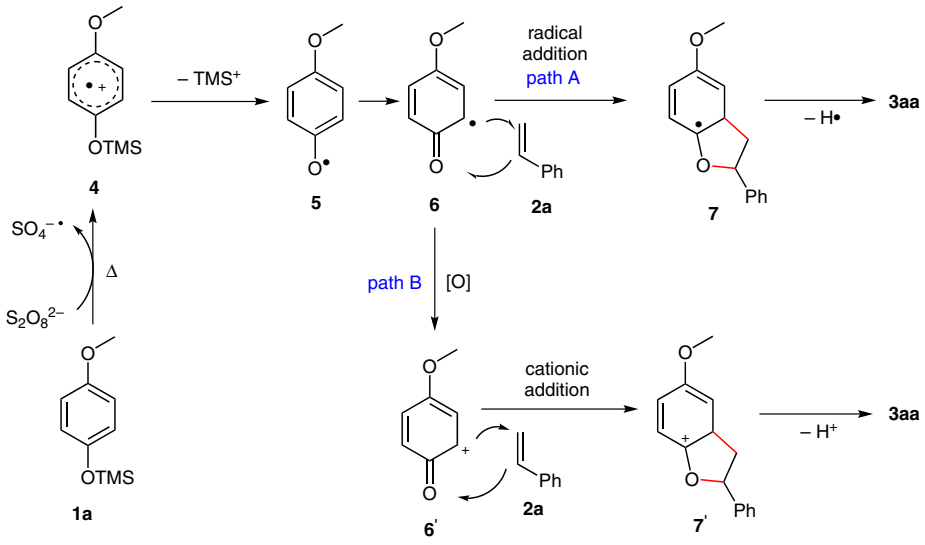
Scheme 3 Study on the limitation of the reaction. *Reagents and conditions*: **1** (0.15 mmol), **2** (0.6 mmol), $Na_2S_2O_8$ (0.45 mmol), MeCN (0.1 M).

According to previous reports, oxidation utilizing persulfate ($S_2O_8^{2-}$) is known to involve radical processes.[9,14] To gain preliminary mechanistic information about this transformation, a radical trapping experiment was performed by addition of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO, 1.5 equiv) to the system of **1a** and **2a** (Equation 3); after 72 hours, three products including a small amount of **3aa** were separated by flash chromatography on silica gel. No feature signals of the TEMPO fragment were observed when analyzing the 4-methoxyphenol or styrene fragments by NMR of the other two products. The failure to trap radical intermediate with TEMPO was not sufficient to prove a non-radical addition process, because of the possibility that the oxidative cyclization took place immediately after the phenoxyl radical had been generated.[15]



Equation 3 Control experiment by addition of TEMPO

Therefore, a possible mechanism for this reaction is presented in Scheme 4. When heated, $S_2O_8^{2-}$ obtains an electron from **1a** and is reduced to $SO_4^{\bullet-}$. The generated radical cation **4** undergoes TMS^+ elimination and leads to a neutral phenoxyl radical **5**. Then the radical is transferred from an O-radical **5** to C-radical **6**, which could subsequently undergo [3+2] radical addition with styrene **2a** to afford the cyclic



Scheme 4 Proposed mechanism

radical intermediate **7**, as shown in path A; a hydrogen atom is then displaced to generate the final product **3aa**. Such a hydrogen atom displacement might lead to C=C bond reduction product **3ae″** (Equation 1). Alternatively, as path B shows, intermediate **6** would be further oxidized to give cation **6′**, which is then intercepted by styrene (**2a**) to form a carbon-centered cation intermediate **7′**. Finally, dihydrobenzofuran **3aa** is delivered by H^+ elimination.

In summary, we have demonstrated a benign and metal-free oxidative [3+2] cross-coupling reaction of phenols with alkenes for the preparation of dihydrobenzofurans. A variety of alkenes that tolerate electronic and steric effects served as suitable nucleophiles to give the corresponding cycloadducts. The features of this approach are its simple operation and mild reaction conditions. Notably, sodium persulfate is an inexpensive, efficient, and environmentally friendly oxidant. The naturally occurring product corsifuran A was synthesized in a single step using this protocol.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker AV-400 spectrometer in $CDCl_3$. For ^{1}H NMR (400 MHz), TMS served as internal standard (δ = 0 ppm). For ^{13}C NMR (100 MHz), $CDCl_3$ was used as internal standard (δ = 77.23 ppm) and spectra were obtained with complete proton decoupling. HRMS spectra were recorded on a Bruker Esquire LC mass spectrometer using electrospray ionization.

2-Aryl-5-methoxy-2,3-dihydrobenzofurans 3; General Procedure

To a 10-mL round-bottomed flask equipped with magnetic stir bar was charged with TMS-protected phenol **1** (0.15 mmol), alkene **2** (0.6 mmol), $Na_2S_2O_8$ (0.45 mmol), and dried MeCN (1.5 mL); the flask put under vacuum and purged with N_2 (3 ×). The mixture was heated at 50 °C until consumption of starting material ceased (monitored by TLC). The mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography to give the final product.

5-Methoxy-2-phenyl-2,3-dihydrobenzofuran (3aa)7a

Colorless oil; yield: 24 mg (72%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.30 (m, 5 H), 6.83–6.73 (m, 2 H), 6.70 (dd, *J* = 8.6, 2.6 Hz, 1 H), 5.74 (t, *J* = 8.8 Hz, 1 H), 3.77 (s, 3 H), 3.60 (dd, *J* = 15.7, 9.3 Hz, 1 H), 3.20 (dd, *J* = 15.7, 8.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.33, 153.81, 142.04, 128.63, 127.99, 127.51, 125.77, 113.04, 111.23, 109.21, 84.24, 56.06, 38.89.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{15}O_2$: 227.1066; found: 227.1027.

5-Methoxy-2-(*p*-tolyl)-2,3-dihydrobenzofuran (3ab)7a

Colorless solid; yield: 24 mg (69%); mp 62–63 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.28 (m, 2 H), 7.18 (d, *J* = 7.8 Hz, 2 H), 6.77 (d, *J* = 10.7 Hz, 2 H), 6.70 (d, *J* = 11.1 Hz, 1 H), 5.70 (t, *J* = 8.8 Hz, 1 H), 3.77 (s, 3 H), 3.57 (dd, *J* = 15.7, 9.3 Hz, 1 H), 3.19 (dd, *J* = 15.7, 8.2 Hz, 1 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.27, 153.84, 138.97, 137.77, 129.29, 127.66, 125.82, 113.01, 111.22, 109.19, 84.27, 56.06, 38.83, 21.16.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}O_2$: 241.1229; found: 241.1221.

5-Methoxy-2-(*o*-tolyl)-2,3-dihydrobenzofuran (3ac)

Colorless oil; yield: 23 mg (65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.42 (m, 1 H), 7.19 (d, *J* = 3.6 Hz, 3 H), 6.80 (d, *J* = 8.6 Hz, 1 H), 6.76 (s, 1 H), 6.71 (dd, *J* = 8.5, 2.6 Hz, 1 H), 5.92 (t, *J* = 8.8 Hz, 1 H), 3.76 (s, 3 H), 3.63 (dd, *J* = 15.6, 9.5 Hz, 1 H), 3.07 (dd, *J* = 15.5, 8.2 Hz, 1 H), 2.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.31, 153.87, 140.29, 134.19, 130.50, 127.60, 127.35, 126.26, 124.99, 113.06, 111.29, 109.21, 81.74, 56.06, 37.90, 19.22.

GC-MS (EI): *m*/*z* = 240.1, 239.1, 211.1, 165.1, 91.1, 28.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}O_2$: 241.1229; found: 241.1186.

2-(4-*tert*-Butylphenyl)-5-methoxy-2,3-dihydrobenzofuran (3ad)[7a]

Pale yellow solid; yield: 22 mg (52%); mp 46–47 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 8.3 Hz, 2 H), 7.33 (d, *J* = 8.3 Hz, 2 H), 6.80–6.73 (m, 2 H), 6.72–6.67 (m, 1 H), 5.71 (t, *J* = 8.7 Hz, 1 H), 3.76 (d, *J* = 6.2 Hz, 3 H), 3.57 (dd, *J* = 15.7, 9.3 Hz, 1 H), 3.22 (dd, *J* = 15.7, 8.2 Hz, 1 H), 1.31 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.25, 153.83, 151.07, 138.84, 127.70, 125.68, 125.55, 113.00, 111.22, 109.19, 84.21, 56.06, 38.61, 34.58, 31.33.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{23}O_2$: 283.1698; found: 283.1695.

5-Methoxy-2-(4-vinylphenyl)-2,3-dihydrobenzofuran (3ae)

Pale yellow oil; yield: 18 mg (50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (ddd, *J* = 28.3, 13.8, 6.1 Hz, 4 H), 6.77 (dt, *J* = 10.1, 5.0 Hz, 2 H), 6.74–6.64 (m, 2 H), 5.74 (ddd, *J* = 12.6, 9.3, 3.7 Hz, 2 H), 5.25 (dd, *J* = 10.9, 3.9 Hz, 1 H), 3.77 (s, 3 H), 3.64–3.55 (m, 1 H), 3.19 (dt, *J* = 15.6, 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.28, 153.72, 136.38, 127.47, 126.45, 125.98, 114.08, 113.00, 111.18, 109.22, 84.02, 56.03, 38.83.

GC-MS (EI): *m*/*z* = 252.2, 237.2, 220.2, 165.1, 152.1, 77.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{16}O_2Na$: 275.1043; found: 275.1037.

5-Methoxy-2-(4-methoxyphenyl)-2,3-dihydrobenzofuran (3af)1a

Pale yellow oil; yield: 15 mg (38%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 8.6 Hz, 2 H), 6.90 (d, *J* = 8.6 Hz, 2 H), 6.83–6.63 (m, 3 H), 5.68 (t, *J* = 8.8 Hz, 1 H), 3.81 (s, 3 H), 3.77 (s, 3 H), 3.55 (dd, *J* = 15.8, 9.2 Hz, 1 H), 3.19 (dd, *J* = 15.7, 8.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.48, 154.25, 153.75, 133.95, 127.72, 127.30, 114.02, 113.00, 111.20, 109.18, 84.19, 56.06, 55.33, 38.73.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}O_3$: 257.1178; found: 257.1182.

5-Methoxy-2-(3-methoxyphenyl)-2,3-dihydrobenzofuran (3ag)

Colorless oil; yield: 16 mg (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 7.9 Hz, 1 H), 6.97 (d, *J* = 8.5 Hz, 2 H), 6.87–6.83 (m, 1 H), 6.78 (d, *J* = 8.2 Hz, 2 H), 6.70 (d, *J* = 8.6 Hz, 1 H), 5.71 (t, *J* = 8.7 Hz, 1 H), 3.80 (s, 3 H), 3.77 (s, 3 H), 3.59 (dd, *J* = 14.9, 10.2 Hz, 1 H), 3.19 (dd, *J* = 15.7, 8.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.86, 154.34, 153.78, 143.68, 129.72, 127.47, 118.01, 113.45, 113.05, 111.22, 111.26, 109.23, 84.09, 56.06, 55.27, 38.88.

GC-MS (EI): *m*/*z* = 256.1, 239.2, 225.2, 181.1, 152.1, 115.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}O_3$: 257.1178; found: 257.0991.

2-(4-Bromophenyl)-5-methoxy-2,3-dihydrobenzofuran (3ah)

Pale yellow oil; yield: 16 mg (35%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (dd, *J* = 24.5, 8.4 Hz, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H), 7.31 (s, 1 H), 6.79 (s, 1 H), 6.76–6.70 (m, 1 H), 5.72 (t, *J* = 8.7 Hz, 1 H), 3.79 (s, 3 H), 3.63 (dd, *J* = 15.4, 9.2 Hz, 1 H), 3.15 (dd, *J* = 15.5, 8.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.47, 153.58, 141.17, 132.47, 131.74, 130.98, 127.44, 113.16, 111.24, 109.28, 83.43, 56.05, 38.87.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{14}BrO_2$: 305.0177; found: 305.0164.

2-(4-Fluorophenyl)-5-methoxy-2,3-dihydrobenzofuran (3ai)

Colorless oil; yield: 15 mg (41%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (dd, *J* = 8.6, 5.4 Hz, 2 H), 7.03 (s, 2 H), 6.77 (d, *J* = 8.6 Hz, 2 H), 6.70 (dd, *J* = 8.5, 2.2 Hz, 1 H), 5.71 (t, *J* = 8.8 Hz, 1 H), 3.77 (s, 3 H), 3.59 (dd, *J* = 15.7, 9.3 Hz, 1 H), 3.16 (dd, *J* = 15.7, 8.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.70, 154.40, 153.59, 127.60, 127.52, 115.62, 115.40, 113.09, 111.21, 109.25, 83.61, 56.05, 38.93.

GC-MS (EI): *m*/*z* = 244.1, 229.1, 211.1, 183.1, 109.1, 55.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{14}FO_2$: 245.0978; found: 245.0979.

8-Methoxy-9b,10-dihydro-4b*H*-benzo[*b*]indeno[2,1-*d*]furan (3aj)

Pale yellow oil; yield: 14 mg (38%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (t, *J* = 8.60 Hz, 1 H), 7.28–7.21 (m, 3 H), 6.81 (s, 1 H), 6.65–6.64 (m, 2 H), 6.18 (d, *J* = 8.23 Hz, 1 H), 4.28 (t, *J* = 17.23 Hz, 1 H), 3.75 (s, 3 H), 3.51 (dd, *J* = 8.58, 8.56 Hz, 1 H), 3.20 (dd, *J* = 1.34, 1.38 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.38, 152.99, 142.17, 140.91, 131.83, 129.23, 127.26, 125.90, 125.09, 113.51, 110.88, 109.81, 90.73, 56.06, 45.27, 38.97.

GC-MS (EI): *m*/*z* = 238.2, 223.1, 207.2, 165.2, 152.1, 115.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{15}O_2$: 239.1072; found: 239.0994.

5-Methoxy-2-methyl-2-phenyl-2,3-dihydrobenzofuran (3ak)7a

Pale yellow solid; yield: 22 mg (61%); mp 53–54 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 7.4 Hz, 2 H), 7.34 (t, *J* = 7.6 Hz, 2 H), 7.25 (d, *J* = 4.8 Hz, 1 H), 6.79 (d, *J* = 8.5 Hz, 1 H), 6.69 (dd, *J* = 12.4, 3.9 Hz, 2 H), 3.74 (s, 3 H), 3.41 (d, *J* = 15.6 Hz, 1 H), 3.34 (d, *J* = 15.5 Hz, 1 H), 1.76 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.16, 153.07, 146.90, 128.35, 127.47, 127.01, 124.54, 113.03, 111.38, 109.40, 89.19, 56.03, 45.17, 29.23.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}O_2$: 241.1223; found: 241.1217.

2-Cyclopropyl-5-methoxy-2-phenyl-2,3-dihydrobenzofuran (3al)

Colorless oil; yield: 27 mg (70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.6 Hz, 2 H), 7.33 (t, *J* = 7.6 Hz, 2 H), 7.26–7.22 (m, 1 H), 6.80–6.55 (m, 3 H), 3.73 (s, 3 H), 3.45 (d, *J* = 15.7 Hz, 1 H), 3.39 (d, *J* = 16.0 Hz, 1 H), 1.51–1.40 (m, 1 H), 0.57–0.48 (m, 2 H), 0.48–0.40 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.07, 153.41, 146.15, 128.12, 127.59, 127.05, 125.23, 112.89, 111.15, 109.00, 90.33, 55.99, 43.24, 21.63, 1.79, 1.35.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{19}O_2$: 267.1385; found: 267.1384.

5-Methoxy-3-methyl-2-(*p*-tolyl)-2,3-dihydrobenzofuran (3am)

Colorless oil; yield: 19 mg (50%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 7.9 Hz, 2 H), 6.78–6.73 (m, 1 H), 6.70 (d, *J* = 7.5 Hz, 2 H), 5.10 (d, *J* = 8.9 Hz, 1 H), 3.78 (s, 3 H), 3.45–3.35 (m, 1 H), 2.36 (s, 3 H), 1.39 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.44, 153.36, 137.99, 137.80, 133.09, 129.28, 126.15, 112.92, 110.13, 109.35, 92.69, 56.07, 45.85, 21.19, 17.76.

GC-MS (EI): *m*/*z* = 254.2, 239.1, 211.1, 165.1, 115.1, 91.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{19}O_2$: 255.1385; found: 255.1387.

5-Methoxy-2-(4-methoxyphenyl)-3-methyl-2,3-dihydrobenzofuran (3an)7a

Colorless oil; yield: 17 mg (43%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 8.6 Hz, 2 H), 6.93–6.90 (m, 2 H), 6.77–6.69 (m, 3 H), 5.08 (d, *J* = 9.1 Hz, 1 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 3.47–3.36 (m, 1 H), 1.39 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.66, 154.43, 153.29, 133.13, 132.73, 127.65, 114.02, 112.89, 110.11, 109.35, 92.61, 56.07, 55.32, 45.69, 17.60.

HRMS (ESI): *m*/*z* [M + K]$^+$ calcd for $C_{17}H_{18}O_3K$: 309.0893; found: 309.0777.

5-Methoxy-2-phenyl-3-propyl-2,3-dihydrobenzofuran (3ao)

Pale yellow oil; yield: 18 mg (45%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (dd, *J* = 13.1, 3.7 Hz, 5 H), 6.74 (dt, *J* = 8.5, 7.3 Hz, 3 H), 5.31 (d, *J* = 6.3 Hz, 1 H), 3.77 (s, 3 H), 3.38 (dd, *J* = 13.1, 6.6 Hz, 1 H), 1.77 (ddd, *J* = 22.7, 11.6, 6.3 Hz, 2 H), 1.47 (dd, *J* = 14.3, 7.2 Hz, 2 H), 0.94 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.30, 153.57, 142.12, 131.62, 128.61, 127.99, 125.93, 112.98, 110.92, 109.18, 90.18, 56.06, 50.93, 37.23, 20.12, 14.17.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{21}O_2$: 269.1542; found: 269.1493.

2-(4-*tert*-Butylphenyl)-7-chloro-5-methoxy-2,3-dihydrobenzofuran (3bd)

Pale yellow oil; yield: 20 mg (42%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 8.4 Hz, 2 H), 7.33 (d, *J* = 8.3 Hz, 2 H), 6.71 (d, *J* = 2.3 Hz, 1 H), 6.68 (s, 1 H), 5.79 (t, *J* = 8.6 Hz, 1 H), 3.75 (s, 3 H), 3.63 (dd, *J* = 16.1, 9.0 Hz, 1 H), 3.28 (dd, *J* = 15.9, 8.0 Hz, 1 H), 1.31 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.49, 151.29, 149.92, 138.10, 128.98, 125.71, 125.58, 113.18, 110.21, 84.70, 56.17, 39.26, 31.32.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{22}ClO_2$: 317.1308; found: 317.1312.

7-Chloro-5-methoxy-2-methyl-2-phenyl-2,3-dihydrobenzofuran (3bk)

Colorless oil; yield: 4 mg (8%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 7.4 Hz, 2 H), 7.35 (t, *J* = 7.7 Hz, 3 H), 6.71 (d, *J* = 2.2 Hz, 1 H), 6.61 (s, 1 H), 3.72 (s, 3 H), 3.48–3.43 (m, 2 H), 1.81 (s, 3 H).

Data are consistent with literature values.[10]

2-(4-Ethylphenyl)-5-methoxy-2,3-dihydrobenzofuran (3ae″)

Pale yellow oil; yield: 7 mg (18%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.27 (m, 1 H), 7.25–7.13 (m, 3 H), 6.80–6.74 (m, 2 H), 6.72–6.67 (m, 1 H), 5.71 (t, *J* = 8.9 Hz, 1 H), 3.77 (s, 3 H), 3.58 (dd, *J* = 15.9, 9.3 Hz, 1 H), 3.21 (dd, *J* = 15.7, 8.5 Hz, 1 H), 2.65 (q, *J* = 7.6 Hz, 2 H), 1.25–1.21 (t, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.83, 143.69, 140.88, 127.59, 126.53, 124.35, 122.13, 112.00, 110.20, 108.19, 83.44, 55.05, 37.84, 28.68, 14.52.

GC-MS (EI): *m*/*z* = 254.2, 239.2, 224.1, 211.2, 105.2, 91.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{19}O_2$: 255.1385; found: 255.1401.

Acknowledgment

We are grateful for financial support from China NSFC (Nos. 21272047, 21372055, and 21472030), SKLUWRE (No. 2015DX01), and the Fundamental Research Funds for the Central Universities (Grant No. HIT.BRETIV.201310).

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1380419.

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