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Potassium Persulfate Mediated Oxidative Radical Cyclization of 1,3-Dicarbonyl Compounds with Styrenes for the Synthesis of Dihydrofurans

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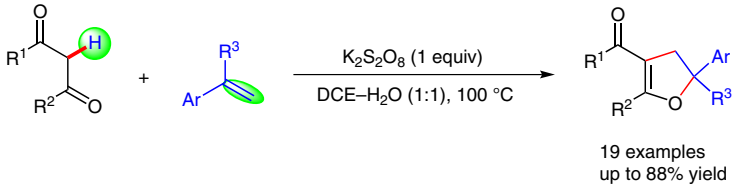

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Abstract A potassium persulfate promoted tandem radical addition/cyclization of 1,3-dicarbonyl compounds with styrenes has been developed. This transition-metal-free procedure provides an efficient approach to a diverse set of substituted dihydrofurans in moderate to good yields.

Key words dicarbonyl compounds, styrenes, free radicals, cyclizations, tandem reactions, furans

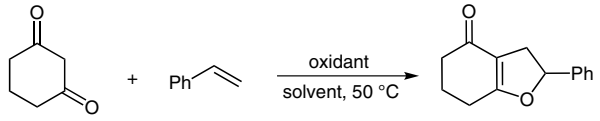
Dihydrofurans are one of the most important classes of heterocycles, and they are widely found in various bioactive natural products and pharmaceuticals.[1] As a result, numerous methods for their preparation have been developed.[2] Classical procedures for the synthesis of dihydrofurans typically involve oxidative cyclization of active methylene compounds with alkenes,[3a–c] allenes,[3d] or aldehydes[3e] in the presence of metal salts or hypervalent iodine reagents.[3f–h] In addition, the coupling/cyclization of activated allenes with organic halides[4a–c] or of terminal alkenes with aryl ketones,[4d] aldehydes,[4e] or benzyl hydrocarbons[4f] in the presence of transition-metal catalysts provides another efficient and convenient route to these heterocycles. Other common methods for the synthesis of dihydrofurans involve cyclizations of enones with various ylides.[5] Recently, Miura and co-workers developed an interesting alkyne cross-coupling reaction that gives fluorescent dihydrofurans in moderate to good yields.[6] However, most of these methods require transition metals, special starting materials, or multistep processes. Therefore, the development of more efficient and environmentally benign procedures leading to dihydrofurans is still highly desirable.[2]

Recently, transition-metal-free coupling reactions have attracted much attention, as they provide beneficial complementary tools for the construction of carbon–carbon and carbon–heteroatom bonds.[7] Potassium persulfate is widely used as an environmentally friendly, easily handled, and efficient oxidant in organic synthesis.[8] Several efforts have also been made to develop potassium persulfate mediated oxidative coupling reactions for C–C bond formation. However, only a few potassium persulfate promoted tandem approaches to valuable heterocycles have been reported.[9] We recently developed a potassium persulfate mediated oxidative spirocyclization of hydroxymethylacrylamides with 1,3-dicarbonyl compounds for the synthesis of spirooxindoles.[9a] Based on this success and results from other groups,[9] we surmised that coupling of nonactivated alkenes, instead of acrylamide, with 1,3-dicarbonyl compounds in the presence of potassium persulfate as an oxidant might provide a practical and reliable method for the synthesis of oxa-heterocycles.[3] Here, we report a potassium persulfate promoted, transition-metal-free, tandem oxidative cyclization of 1,3-dicarbonyl compounds with readily available styrenes to give substituted dihydrofurans.

Initially, we investigated the cyclization of cyclohexane-1,3-dione (**1a**) with styrene (**2a**) under our previous conditions.[9a] Unfortunately, only a trace amount of the desired dihydrofuran **3a** was detected (Table 1, entry 1). To our delight, however, when we used a 1:1 mixture of dichloromethane and water as the solvent, we isolated the expected product **3a** in 48% yield (entry 2). Other solvents such as 1,2-dichloroethane–water, ethyl acetate–water, toluene–water, or chlorobenzene–water were also tested (entries 3–6), and, of these, 1,2-dichloroethane–water gave the best yield. These results implied that a two-phase system favors the cyclization. The use of water as the sole solvent was also found to be appropriate for the reaction, although it gave a somewhat lower yield (entry 7). Note that increasing the

loading of the oxidant to two equivalents did not significantly affect the yield of dihydrofuran **3a** (entry 8). Further optimization studies revealed that potassium persulfate was the most effective oxidant for the reaction (entries 9 and 10). No reaction was observed when Oxone (potassium peroxymonosulfate) was used instead of potassium persulfate (entry 11). When we examined the effect of the temperature, 100 °C was found to be optimal (entries 12–14). Finally, no reaction occurred in the absence of potassium persulfate (entry 15). In an attempt to obtain the corresponding furan product, we tested the oxidant 2,3-dichloro-5,6-dicyano-1,4-benzoquinone for the dehydrogenation of **3a** under various conditions; however, the desired product was not obtained.

Table 1 Optimization of the Reaction Conditions[a]



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

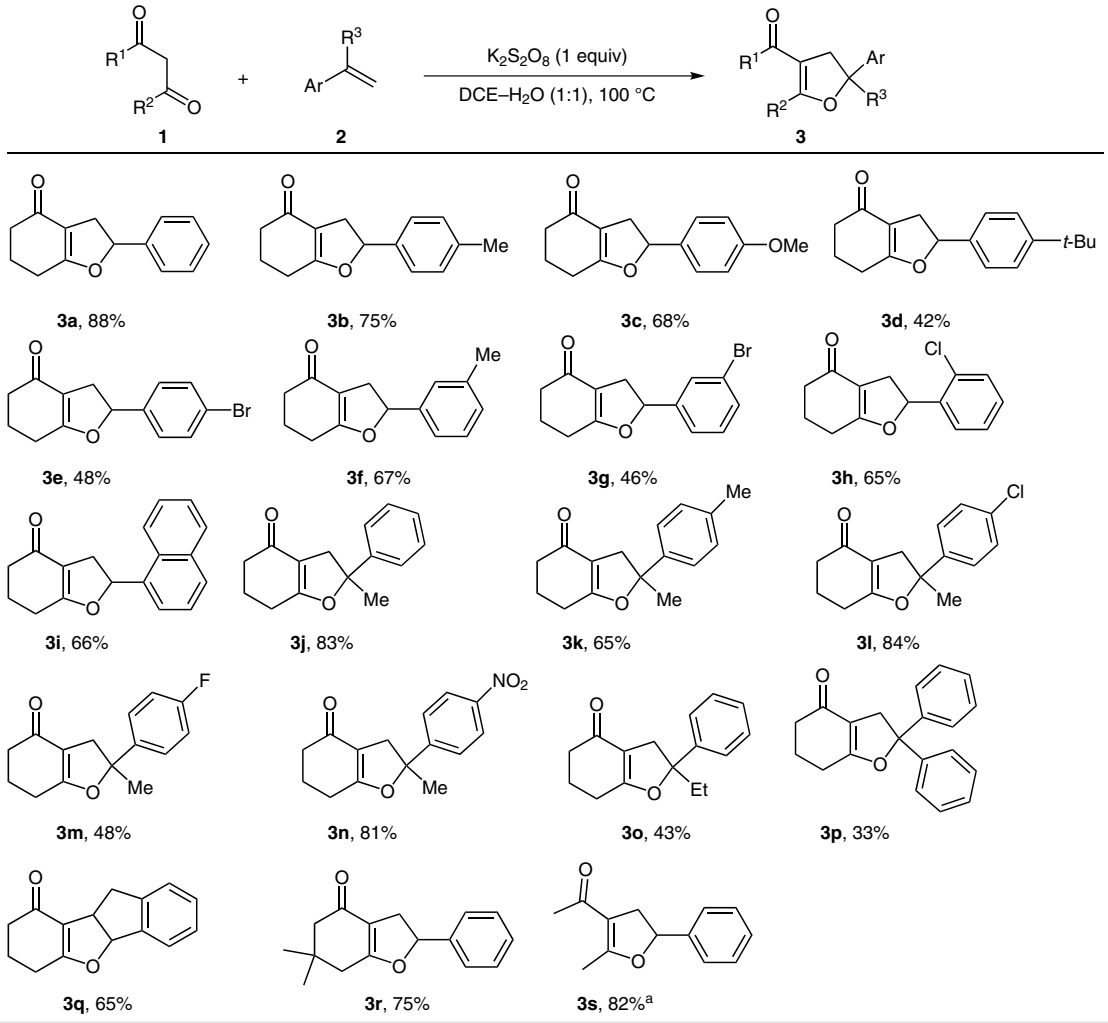
Entry	Oxidant (equiv)	Solvent	Yield[b] (%)
1	$K_2S_2O_8$ (1)	MeCN–H_2O (1:1)	trace
2	$K_2S_2O_8$ (1)	CH_2Cl_2–H_2O (1:1)	48
3	$K_2S_2O_8$ (1)	DCE–H_2O (1:1)	61
4	$K_2S_2O_8$ (1)	EtOAc–H_2O (1:1)	37
5	$K_2S_2O_8$ (1)	toluene–H_2O (1:1)	49
6	$K_2S_2O_8$ (1)	PhCl–H_2O (1:1)	50
7	$K_2S_2O_8$ (1)	H_2O	29
8	$K_2S_2O_8$ (2)	DCE–H_2O (1:1)	62
9	$Na_2S_2O_8$ (1)	DCE–H_2O (1:1)	56
10	$(NH_4)_2S_2O_8$ (1)	DCE–H_2O (1:1)	43
11	Oxone (1)	DCE–H_2O (1:1)	n.r.[c]
12	$K_2S_2O_8$ (1)	DCE–H_2O (1:1)	67[d]
13	$K_2S_2O_8$ (1)	DCE–H_2O (1:1)	88[e] (73)[f]
14	$K_2S_2O_8$ (1)	DCE–H_2O (1:1)	78[g]
15	–	DCE–H_2O (1:1)	n.r.[c]

[a] Reaction conditions: **1a** (0.3 mmol, 1.5 equiv), **2a** (0.2 mmol, 1 equiv), solvent (1 mL), oxidant (1 equiv), 50 °C, 28 h.
[b] Yield of isolated product.
[c] No reaction.
[d] At 80 °C.
[e] At 100 °C.
[f] Yield on a 1 mmol scale.
[g] At 120 °C.

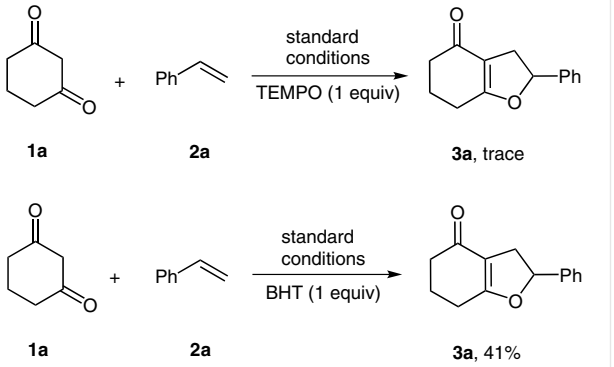
Having identified the optimal reaction conditions, we investigated the substrate scope of this cyclization reaction. As shown in Scheme 1, a wide range of substituents at the *para*-, *meta*-, or *ortho*-position of the styrene were compatible with this transformation (**3b**–**h**). Gratifyingly, styrenes having a bromo substituent were also tolerated under the conditions, and gave the desired products **3e** and **3g** in 48% and 46% yields, respectively. 1-Vinylnaphthalene (**2i**) also reacted smoothly with dione **1a** to afford the corresponding dihydrofuran **3i** in moderate yield. Furthermore, various α-methylstyrenes were also found to be suitable substrates for this reaction, providing the corresponding dihydrofurans **3j**–**n** containing a quaternary carbon center. α-Methylstyrenes with electron-donating or electron-withdrawing groups at the *para*-position of the aromatic ring reacted readily with dione **1a** to give the corresponding dihydrofurans **3j**–**n** in moderate to good yields. Surprisingly, when 4-(trifluoromethyl)styrene was used, only a small amount of the corresponding dihydrofuran was detected, and 82% of the dione **1a** was recovered. Styrenes with an ethyl or phenyl group at the α-position also afforded the desired products **3o** and **3p** in 43% and 33% yields, respectively. Notably, the scope of alkenes was not limited to styrenes, because 1*H*-indene also gave the corresponding cyclized product in good yield (**3q**). When other terminal aliphatic alkenes such as but-3-en-1-ylbenzene or pent-4-en-1-yl benzoate were tested as potential substrates, none of the desired product was obtained, even at 120 °C. Other 1,3-dicarbonyl compounds, such as 5,5-dimethylcyclohexane-1,3-dione and pentane-2,4-dione were also suitable substrate for this tandem cyclization reaction (**3r** and **3s**). Unfortunately, when benzoylacetone was used as substrate, no reaction occurred, possibly as a result of the steric hindrance by the phenyl group; in attempts to prepare the desired cyclization product, a range of catalysts, oxidants, and solvent were tested, but no satisfactory result was obtained. Under the optimized conditions, ethyl acetoacetate afforded a complex mixture containing only a trace amount of the desired product. Finally, no reaction occurred when β-keto aldehydes and malonates were used as substrates in the cyclization reaction under the standard conditions.

Some control experiments were performed to elucidate the mechanism of the cyclization reaction. When a radical-trapping reagent, such as (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) or butylated hydroxytoluene (BHT), was added to a mixture of **1a** and **2a** under the standard conditions (Scheme 2), the reaction was suppressed markedly, indicating that the transformation probably involves a radical process.

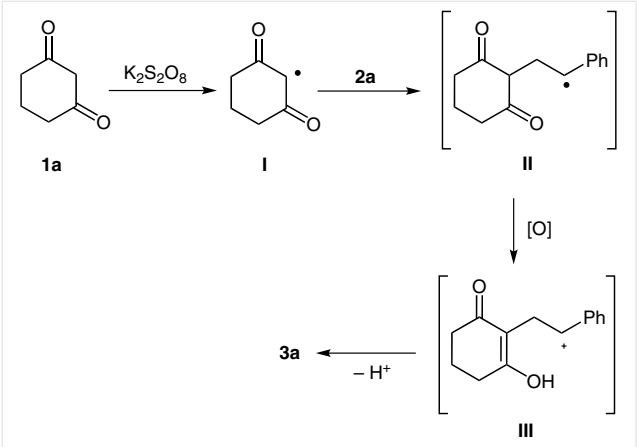
Based on these experimental results and our previous reports,[9a] we proposed the mechanism shown in Scheme 3. Firstly, oxidation of dione **1a** by potassium persulfate generates the corresponding alkyl radical **I**, which attacks the carbon–carbon double bond of styrene (**2a**) to give radical **II**. Secondly, radical **II** is oxidized to the corresponding carbocation **III**,[3] which undergoes an intramolecular cyclization to produce the dihydrofuran **3a**. However, a radical cyclization process, in which radical **II** undergoes a radical 5-*endo*-*trig* cyclization to give the desired product **3a**,[4e,f,10] is also possible.



Scheme 1 Scope of nonactivated alkenes and 1,3-dicarbonyl compounds. *Reagents and conditions*: **1** (0.3 mmol, 1.5 equiv), **2** (0.2 mmol, 1 equiv), DCE–H_2O (1:1; 1 mL), $K_2S_2O_8$ (1 equiv), 100 °C, 28 h. [a] $K_2S_2O_8$ (2.5 equiv) was used.



Scheme 2 Control experiments



Scheme 3 Proposed mechanism

In summary, we have developed a simple transition-metal-free approach for the synthesis of substituted dihydrofurans by a tandem radical addition/cyclization process. This method has the advantages of using commercially available starting materials with nontoxic and inexpensive potassium persulfate as a radical initiator.

All reactions were carried out under N_2 with strict exclusion of air. Column chromatography was carried out on silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Advance III-400 spectrometer in the solvents indicated. Chemical shift are reported in ppm relative to $CDCl_3$ with TMS as internal standard. IR spectra were recorded on a Bruker Tensor 27 spectrometer, and only the major peaks are reported. High-resolution mass spectra were obtained on a Q-TOF micro spectrometer. Styrenes **1** were purchased from TCI, Alfa, or Acros. All other commercially available compounds were used without further purification.

Dihydrofurans 3; General Procedure

A 10 mL, oven-dried, Schlenk-tube was charged with the appropriate 1,3-dicarbonyl compound **1** (0.3 mmol, 1.5 equiv.) and $K_2S_2O_8$ (0.2 mmol, 1.0 equiv.). The tube was evacuated and backfilled with N_2 (three times). A solution of aralkene **2** (0.2 mmol, 1.0 equiv) in DCE–H_2O (1:1; 1 mL) was added from a syringe. The tube was sealed and the mixture was stirred for 28 h at 100 °C. The resulting mixture was diluted with EtOAc (10 mL), and the organic phase was washed successively with H_2O (2 × 10 mL) and brine (10 mL) then dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by column chromatography [silica gel, EtOAc–PE (gradient 1:10 to 1:25)].

2-Phenyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3a)

Colorless oil; yield: 37.7 mg (88%); R_f = 0.3 (EtOAc–PE, 1:3).

IR (KBr): 1634, 1402, 1232, 1180 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.31 (m, 5 H), 5.77–5.72 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.31–3.25 (m, 1 H), 2.90–2.84 (m, 1 H), 2.53–2.41 (m, 2 H), 2.39–2.37 (m, 2 H), 2.12–2.05 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 177.1, 140.6, 128.8, 128.5, 125.8, 113.0, 86.3, 36.4, 33.9, 23.9, 21.7.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{14}NaO_2$: 237.0886; found: 237.0891.

2-(4-Tolyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3b)

White solid; yield: 34.2 mg (75%); mp 75–76 °C; R_f = 0.2 (EtOAc–PE, 1:3).

IR (KBr): 1634, 1401, 1229, 1180 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.18 (m, 4 H), 5.74–5.69 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.29–3.22 (dd, *J* = 14.4, 10.4 Hz, 1 H), 2.91–2.85 (dd, *J* = 14.4, 8.0 Hz, 1 H), 2.51–2.48 (t, *J* = 6.4 Hz, 2 H), 2.41–2.38 (t, *J* = 6.0 Hz, 2 H), 2.36 (s, 3 H), 2.11–2.05 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 177.1, 138.4, 137.5, 129.4, 126.0, 113.0, 86.4, 36.5, 33.8, 24.0, 21.7, 21.2.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{16}NaO_2$: 251.1043; found: 251.1053.

2-(4-Methoxyphenyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3c)

Pale-yellow solid; yield: 33.2 mg (68%); mp 77–79 °C; R_f = 0.2 (EtOAc–PE, 1:3).

IR (KBr): 1631, 1514, 1401, 1249, 1178 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.26 (d, *J* = 8.4 Hz, 2 H), 6.92–6.90 (d, *J* = 8.4 Hz, 2 H), 5.73–5.68 (dd, *J* = 10.4, 8.4 Hz, 1 H), 3.82 (s, 3 H), 3.27–3.21 (m, 1 H), 2.92–2.86 (dd, *J* = 14.4, 8.0 Hz, 1 H), 2.50–2.47 (t, *J* = 6.4 Hz, 2 H), 2.41–2.38 (t, *J* = 6.0 Hz, 2 H), 2.11–2.05 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 177.0, 159.8, 132.4, 127.6, 114.1, 113.0, 86.4, 55.3, 36.5, 33.6, 24.0, 21.7.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{16}NaO_3$: 267.0992; found: 267.1005.

2-(4-*tert*-Butylphenyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3d)

White solid; yield: 22.7 mg (42%); mp 79–81 °C; R_f = 0.4 (EtOAc–PE, 1:3).

IR (KBr): 1633, 1400, 1230, 1181 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.40 (d, *J* = 8.4 Hz, 2 H), 7.29–7.26 (d, *J* = 8.4 Hz, 2 H), 5.75–5.71 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.29–3.23 (m, 1 H), 2.95–2.93 (m, 1 H), 2.51–2.48 (m, 2 H), 2.41–2.38 (m, 2 H), 2.14–2.05 (m, 2 H), 1.32 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 177.1, 151.7, 137.4, 125.9, 125.8, 113.1, 86.4, 36.5, 34.6, 33.6, 31.3, 24.0, 21.8.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{18}H_{23}O_2$: 271.1693; found: 271.1697.

2-(4-Bromophenyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3e)

Colorless oil; yield: 28.0 mg (48%); R_f = 0.1 (EtOAc–PE, 1:3).

IR (KBr): 1636, 1399, 1229, 1180 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.50 (d, *J* = 8.4 Hz, 2 H), 7.21–7.19 (d, *J* = 8.4 Hz, 2 H), 5.72–5.68 (dd, *J* = 10.4, 8.4 Hz, 1 H), 3.31–3.25 (dd, *J* = 14.4, 10.4 Hz, 1 H), 2.84–2.79 (dd, *J* = 14.8, 8.0 Hz, 1 H), 2.53–2.49 (t, *J* = 6.4 Hz, 2 H), 2.41–2.38 (t, *J* = 6.0 Hz, 2 H), 2.12–2.06 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 176.9, 139.7, 131.9, 127.5, 122.4, 112.9, 85.4, 36.5, 34.0, 23.9, 21.7.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{13}BrNaO_2$: 314.9991; found: 315.0000.

2-(3-Tolyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3f)

Yellow sticky oil; yield: 30.6 mg (67%); R_f = 0.3 (EtOAc–PE, 1:3).

IR (KBr): 1634, 1401, 1231, 1180 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.26 (d, *J* = 6.0 Hz, 1 H), 7.17–7.14 (m, 3 H), 5.74–5.69 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.30–3.24 (m, 1 H), 2.91–2.86 (dd, *J* = 14.4, 8.0 Hz, 1 H), 2.53–2.50 (m, 2 H), 2.42–2.37 (m, 5 H), 2.13–2.06 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 177.1, 140.5, 138.6, 129.3, 128.7, 126.6, 123.0, 113.1, 86.5, 36.5, 33.9, 24.0, 21.8, 21.5.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{16}NaO_2$: 251.1043; found: 251.1051.

2-(3-Bromophenyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3g)

Colorless oil; yield: 26.9 mg (46%); R_f = 0.3 (EtOAc–PE, 1:3).

IR (KBr): 1635, 1340, 1230, 1180 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.46 (m, 2 H), 7.29–7.24 (m, 2 H), 5.73–5.69 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.33–3.26 (m, 1 H), 2.86–2.80 (m, 1 H), 2.56–2.52 (m, 2 H), 2.42–2.39 (t, *J* = 6.0 Hz, 2 H), 2.14–2.09 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 176.9, 143.0, 131.5, 130.4, 128.8, 124.4, 122.9, 112.9, 85.2, 36.5, 34.2, 23.9, 21.7.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{14}BrO_2$: 293.0172; found: 293.0172.

2-(2-Chlorophenyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3h)

Colorless oil; yield: 32.3 mg (65%); R_f = 0.4 (EtOAc–PE, 1:3).

IR (KBr): 1640, 1400, 1231, 1180 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.25 (m, 4 H), 6.08–6.03 (dd, *J* = 10.4, 7.6 Hz, 1 H), 3.46–3.40 (dd, *J* = 14.8, 10.8 Hz, 1 H), 2.74–2.68 (dd, *J* = 14.8, 7.6 Hz, 1 H), 2.59–2.56 (t, *J* = 6.4 Hz, 2 H), 2.42–2.38 (m, 2 H), 2.15–2.08 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 176.9, 138.7, 131.5, 129.8, 129.2, 127.1, 126.0, 112.9, 83.0, 36.5, 33.8, 23.8, 21.7.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{14}H_{13}ClNaO_2$: 271.0496; found: 271.0506.

2-(1-Naphthyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3i)

White solid; yield: 34.9 mg (66%); mp 118–120 °C; R_f = 0.2 (EtOAc–PE, 1:3).

IR (KBr): 1635, 1401, 1233, 1180 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.89 (m, 1 H), 7.85–7.83 (m, 2 H), 7.57–7.45 (m, 4 H), 6.45–6.40 (dd, *J* = 10.8, 8.0 Hz, 1 H), 3.53–3.46 (m, 1 H), 2.96–2.90 (m, 1 H), 2.64–2.60 (m, 2 H), 2.45–2.41 (m, 2 H), 2.18–2.11 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 177.1, 136.0, 133.9, 129.7, 129.0, 128.8, 126.5, 125.9, 125.2, 122.9, 122.3, 113.2, 84.2, 36.5, 34.0, 24.0, 21.8.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{18}H_{16}NaO_2$: 287.1043; found: 287.1055.

2-Methyl-2-phenyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3j)

Yellow sticky oil; yield: 37.9 mg (83%); R_f = 0.4 (EtOAc–PE, 1:3).

IR (KBr): 1634, 1400, 1252, 1184 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.36 (m, 4 H), 7.31–7.26 (m, 1 H), 3.11–3.08 (d, *J* = 14.4 Hz, 1 H), 3.02–2.99 (d, *J* = 14.4 Hz, 1 H), 2.55–2.52 (m, 2 H), 2.39–2.35 (m, 2 H), 2.12–2.05 (m, 2 H), 1.72 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.7, 175.9, 145.6, 128.5, 127.5, 124.2, 112.6, 92.6, 40.5, 36.4, 29.7, 24.1, 21.7.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{16}NaO_2$: 251.1043; found: 251.1052.

2-Methyl-2-(4-tolyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3k)

Colorless sticky oil; yield: 31.5 mg (65%); R_f = 0.4 (EtOAc–PE, 1:3).

IR (KBr): 1635, 1400, 1251, 1184 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.26 (d, *J* = 8.4 Hz, 2 H), 7.19–7.17 (d, *J* = 8.0 Hz, 2 H), 3.11–3.08 (d, *J* = 14.4 Hz, 1 H), 3.01–2.97 (d, *J* = 14.4 Hz, 1 H), 2.54–2.51 (t, *J* = 6.0 Hz, 2 H), 2.40–2.36 (m, 5 H), 2.12–2.05 (m, 2 H), 1.72 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.7, 175.9, 142.6, 137.2, 129.1, 124.2, 112.6, 92.6, 40.5, 36.4, 29.6, 24.1, 21.7, 21.0.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{16}H_{18}NaO_2$: 265.1199; found: 265.1213.

2-(4-Chlorophenyl)-2-methyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3l)

Colorless oil; yield: 44.0 mg (84%); R_f = 0.3 (EtOAc–PE, 1:3).

IR (KBr): 1637, 1400, 1250, 1184 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.28 (m, 4 H), 3.06–2.96 (m, 2 H), 2.54–2.50 (m, 2 H), 2.39–2.35 (m, 2 H), 2.11–2.04 (m, 2 H), 1.69 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 175.7, 144.1, 133.3, 128.6, 125.8, 112.5, 92.0, 40.5, 36.4, 29.7, 24.0, 21.7.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{16}ClO_2$: 263.0833; found: 263.0844.

2-(4-Fluorophenyl)-2-methyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3m)

Pale-yellow oil; yield: 23.6 mg (48%); R_f = 0.3 (EtOAc–PE, 1:3).

IR (KBr): 1636, 1511, 1400, 1250 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.31 (m, 2 H), 7.06–7.02 (m, 2 H), 3.07–2.97 (m, 2 H), 2.54–2.50 (m, 2 H), 2.39–2.35 (m, 2 H), 2.10–2.06 (m, 2 H), 1.70 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 175.7, 162.0 (d, *J* = 244.9 Hz), 141.4 (d, *J* = 3.0 Hz), 126.1 (d, *J* = 8.1 Hz), 115.3 (d, *J* = 21.3 Hz), 112.6, 92.1, 40.6, 36.4, 29.7, 24.1, 21.7.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{15}FNaO_2$: 269.0948; found: 269.0946.

2-Methyl-2-(4-nitrophenyl)-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3n)

Yellow oil; yield: 44.2 mg (81%); R_f = 0.2 (EtOAc–PE, 1:3).

IR (KBr): 1638, 1520, 1400, 1249 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24–8.22 (d, *J* = 8.8 Hz, 2 H), 7.55–7.53 (d, *J* = 8.8 Hz, 2 H), 3.11–3.01 (m, 2 H), 2.58–2.54 (m, 2 H), 2.40–2.36 (m, 2 H), 2.14–2.10 (m, 2 H), 1.74 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.5, 175.4, 152.7, 147.2, 125.3, 123.9, 112.4, 91.6, 40.6, 36.4, 29.8, 23.7, 21.6.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{15}H_{15}NNaO_4$: 296.0893; found: 296.0892.

2-Ethyl-2-phenyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3o)

Colorless oil; yield: 20.8 mg (43%); R_f = 0.3 (EtOAc–PE, 1:3).

IR (KBr): 1638, 1450, 1248, 1139 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 4 H), 7.27–7.25 (m, 1 H), 3.05–3.04 (m, 2 H), 2.55–2.51 (m, 2 H), 2.39–2.28 (m, 2 H), 2.10–2.05 (m, 2 H), 2.03–1.93 (m, 2 H), 0.84–0.81 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 176.2, 144.5, 128.3, 127.3, 124.7, 112.8, 95.5, 38.5, 36.4, 35.8, 23.9, 21.7, 8.0.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{16}H_{18}NaO_2$: 265.1199; found: 265.1188.

2,2-Diphenyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3p)

Colorless sticky oil; yield: 19.1 mg (33%); R_f = 0.5 (EtOAc–PE, 1:3).

IR (KBr): 1639, 1397, 1245, 1181 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 7 H), 7.30–7.26 (m, 3 H), 3.57–3.56 (t, *J* = 1.6 Hz, 2 H), 2.61–2.58 (m, 2 H), 2.39–2.36 (t, *J* = 6.4 Hz, 2 H), 2.13–2.06 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 175.6, 144.5, 128.4, 127.8, 125.7, 112.9, 95.4, 40.6, 36.4, 24.0, 21.7.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{20}H_{18}NaO_2$: 313.1199; found: 313.1204.

4b,6,7,8,9b,10-Hexahydro-9*H*-benzo[*b*]indeno[2,1-*d*]furan-9-one (3q)

Pale-yellow solid; yield: 29.4 mg (65%); mp 103–104 °C; R_f = 0.4 (EtOAc–PE, 1:3).

IR (KBr): 1639, 1397, 1246, 1181 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.48 (d, *J* = 7.2 Hz, 1 H), 7.36–7.26 (m, 3 H), 6.21–6.18 (d, *J* = 8.8 Hz, 1 H), 4.05–4.01 (td, *J* = 8.8, 1.2 Hz, 1 H), 3.39–3.32 (dd, *J* = 16.8, 8.4 Hz, 1 H), 3.20–3.16 (dd, *J* = 16.8, 2.0 Hz, 1 H), 2.47–2.29 (m, 4 H), 2.05–1.94 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 176.5, 143.4, 139.4, 129.8, 127.0, 125.8, 125.6, 116.8, 93.3, 41.8, 37.4, 36.7, 24.0, 21.6.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{15}H_{14}NaO_2$: 249.0886; found: 249.0897.

6,6-Dimethyl-2-phenyl-3,5,6,7-tetrahydro-1-benzofuran-4(2*H*)-one (3r)

Yellow sticky oil; yield: 36.3 mg (75%); R_f = 0.4 (EtOAc–PE, 1:3).

IR (KBr): 1636, 1402, 1220, 1144 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 5 H), 5.79–5.74 (dd, *J* = 10.4, 8.0 Hz, 1 H), 3.32–3.26 (dd, *J* = 14.4, 10.4 Hz, 1 H), 2.90–2.85 (dd, *J* = 14.4, 7.6 Hz, 1 H), 2.37 (s, 2 H), 2.27 (s, 2 H), 1.14 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.7, 176.0, 140.7, 128.8, 128.5, 125.8, 111.4, 86.5, 50.9, 37.8, 34.1, 33.8, 28.8, 28.5.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{16}H_{18}NaO_2$: 265.1199; found: 265.1206.

1-(2-Methyl-5-phenyl-4,5-dihydrofuran-3-yl)ethanone (3s)

Colorless oil; yield: 33.1 mg (82%); R_f = 0.4 (EtOAc–PE, 1:5).

IR (KBr): 1719, 1373, 1236 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.31 (m, 5 H), 5.63–5.58 (dd, *J* = 10.4, 8.4 Hz, 1 H), 3.43–3.37 (ddd, *J* = 12.4, 10.8, 1.6 Hz, 1 H), 3.01–2.95 (ddd, *J* = 9.6, 8.4, 1.6 Hz, 1 H), 2.32 (t, *J* = 1.6 Hz, 3 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.8, 167.8, 141.6, 129.1, 128.6, 126.0, 112.2, 83.5, 39.1, 29.9, 15.4.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{13}H_{14}NaO_2$: 225.0886; found: 225.0888.

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Supporting Information

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