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Palladium-Catalyzed Oxidative Cyclization of 3-Phenoxyacrylates: An Approach To Construct Substituted Benzofurans from Phenols

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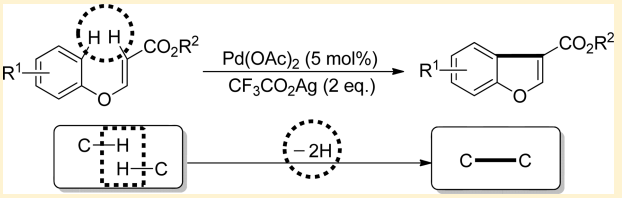
Supporting Information

ABSTRACT: In this paper, a novel and applicable synthesis of benzofurans from commercially available phenols and propiolate through the direct oxidative cyclization has been developed. In the presence of $Pd(OAc)_2/PPh_3$ and CF_3CO_2Ag, (*E*)-type 3-phenoxyacrylates underwent reaction smoothly to generate the corresponding benzofurans in good yields in benzene at 110 °C under the air pressure. In addition, this transformation of phenols into benzofurans can also be carried out in one pot. The process was simple and efficient. A tentative mechanism of palladium-catalyzed oxidative cyclization of 3-phenoxyacrylates was proposed.



Benzofuran is one of the important structural units and is widely found in important heterocyclic biological and medical compounds. Many efforts have been made to achieve efficient preparation of this motif.[1] The most powerful tool is undoubtedly the palladium-catalyzed annulation reaction, in which prefunctionalized substrates, such as *o*-alkynyl- or -halophenol, were generally utilized through Heck and Sonagashira reactions.[2] However, to the best of our knowledge, simple phenols without halogen and alkyne substituents have rarely been used as starting materials to directly construct those derivatives.[3] Recently, an oxidative Pechmann condensation reaction of the simple phenols and β-keto esters was developed by Li, and the reaction could proceed to generate polysubstituted benzofurans by using iron catalysts in the presence of an oxidant.[4]

In recent years, transition-metal-catalyzed C−H activation and functionalization for the atom- and step-economical synthesis of functional molecules have attracted tremendous attention in both academia and industry.[5] The advantages of this method are high efficiency, low cost, and environmental friendliness.[6] Several transition metals, such as Pd-,[7] Rh-,[8] Ru-,[9] and Fe-catalyzed[10] C−H bond activation and functionalization have been widely developed. Most recently, an efficient synthesis of functionalized indoles from commercially available anilines by palladium- and iron-catalyzed intramolecular oxidative cyclization via direct oxidative C−C coupling by the selective activation of C−H bonds has been reported.[11] In this paper, we wish to report a novel and efficient palladium-catalyzed direct C−H functionalization of 3-phenoxyacrylates. The reactions generated the corresponding benzofurans in good yields.

As the substrates, 3-phenoxyacrylates were readily prepared through a one-step procedure.[12] According to the literature, the reaction of various phenols with ethyl propiolate and methyl propiolate in the presence of a catalytic amount of DABCO (10 mol %) proceeded smoothly in dichloromethane for 15 min at room temperature to give the desired conjugate addition products in excellent yields. The ^{1}H NMR spectroscopic analysis of the crude product showed that the corresponding mixture of a pair of separable *Z*- and *E*-isomers was obtained with a majority of the *E*-isomer. Fortunately, the *E*-isomer could be facilely isolated by flash chromatography on a silica column. In some cases, the reaction completely gave the *E*-isomer.

Initial attempts for the synthesis of benzofurans from (*E*)-3-phenoxyacrylates applied the synthetic methods of indoles with $Pd(OAc)_2$ or $FeCl_3$ used as catalyst.[11] However, no desired benzofuran was obtained. Thus, it is necessary to optimize the cyclization reaction conditions. At first, the effect of solvents on the model reaction (ethyl 3-phenoxyacrylate as model substrate) was examined, and the results are summarized in Table 1. When the model reaction was carried out in the presence of $Pd(OAc)_2$ (5 mmol %), PPh_3 (5 mmol %), and CF_3CO_2Ag (2.0 equiv), a significant solvent effect was observed. Among the solvents tested in Table 1, benzene was found to be the best (Table 1, entry 1). A good yield of the desired product was also obtained when chlorobenzene or toluene was used as solvent (Table 1, entries 2 and 3). However, when the reactions were performed in 1,2-dichloroethane (DCE) and 1,4-dioxane, 47% and 41% yields of the corresponding products were obtained, respectively (Table 1, entries 4 and 5). Meanwhile, only a trace amount of the product was obtained when the reaction was performed in MeCN or THF (Table 1, entries 6 and 7). Unfortunately, no desired product was isolated when the reaction was carried out in

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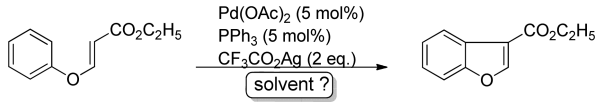
Table 1. Effect of Solvent on the Cyclization Reaction[a]



entry	solvent/temp (°C)	yield[b] (%)
1	benzene/110	81
2	chlorobenzene/110	75
3	toluene/110	71
4	DCE/80	47
5	dioxane/100	41
6	MeCN/80	<10
7	THF/70	<10

[a] Reaction conditions: (*E*)-ethyl 3-phenoxyacrylate (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.05 mmol), CF_3CO_2Ag (2.0 mmol), solvent (2.0 mL), under air, 24 h. [b] Isolated yields.

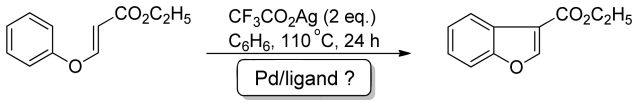
N,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), *N*-methyl-2-pyrrolidone (NMP), or EtOH.

We next screened the effect of palladium source and ligand on the cyclization reaction of model substrate by using CF_3CO_2Ag (2.0 equiv) as oxidant at 110 °C in benzene, and the results are summarized in Table 2. The model reaction could be catalyzed by Pd^{II} salts, or Pd^0 complexes, such as $Pd(OAc)_2$, $PdCl_2$, $Pd(PCy_3)_2Cl_2$, $Pd(MeCN)_2Cl_2$, $Pd(PPh_3)_2Cl_2$, and $Pd(PPh_3)_4$ in the absence of additional ligand. From Table 2, the reactivity of Pd catalytic system decreases in the following order for the cyclization reaction: $Pd(OAc)_2/PPh_3$ > $Pd(OAc)_2$/dppf ≈ $Pd(PPh_3)_4$ ≈ $Pd(OAc)_2/PCy_3$ > $Pd(PPh_3)_2Cl_2$ ≈ $Pd(PCy_3)_2Cl_2$ > $Pd(MeCN)_2Cl_2/PPh_3$ ≈ $PdCl_2/PPh_3$ > $Pd(OAc)_2$ > $PdCl_2$ (Table 2, entries 1−10). It is evident that the *P*-ligand, such as $(C_6H_5)_3P$, $(C_6H_{11})_3P$, or 1,1′-bis(diphenylphosphino)ferrocene (DPPF), could accelerate the reaction to a certain extent. However, *N*-ligands such as 1,10-phenanthroline could not assist in palladium-catalyzing the model reaction and, conversely, restrained the reactivity of catalyst completely (Table 2, entry 11). But, $FeCl_3$ and $FeCl_3 \cdot 6H_2O$ failed to catalyze the reaction, even in the presence of PPh_3.

A variety of oxidants were examined for their effects on the model cyclization reaction. To our delight, the model reaction proceeded smoothly and generated the desired product in 81% yield, representing one of the best results when 2 equiv of CF_3CO_2Ag was used as oxidant. It was found that $C_6H_5I(OAc)_2$ was inferior and generated the desired product in 48% yield. Unfortunately, other oxidants, such as Ag_2O, Ag_2CO_3, $CuCl_2 \cdot 2H_2O$, $Cu(OAc)_2$, 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), *tert*-butyl hydroperoxide (TBHP), $K_2S_2O_8$, $(t\text{-}C_4H_9O)_2$, $(C_6H_5COO)_2$, I_2, and O_2 were no longer the effective oxidants in this reaction. With respect to the oxidant loading, 2 equiv of CF_3CO_2Ag was found to be optimal. During the course of further optimization of the reaction temperature and time, the reaction was generally completed within 24 h when it was performed at 110 °C using $Pd(OAc)_2/PPh_3$ (5 mmol %) and CF_3CO_2Ag (2.0 equiv) in benzene.

On the basis of the previously optimized reaction conditions, the scope of this cyclization reaction was evaluated. A variety of (*E*)-type 3-phenoxyacrylate derived from phenol or substituted phenol and ethyl propiolate were examined for the reaction, and the results are outlined in Table 3. As can be seen from Table 3, phenol and substituted phenols, with either electron-donating or

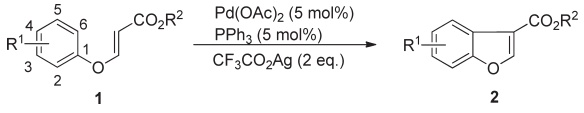
Table 2. Effect of Palladium and Ligand on the Reaction[a]



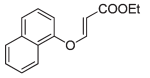
entry	palladium/ligand	yield[b] (%)
1	$Pd(OAc)_2$	50
2	$Pd(OAc)_2/PPh_3$	81
3	$PdCl_2$	37
4	$PdCl_2/PPh_3$	53
5	$Pd(MeCN)_2Cl_2/PPh_3$	55
6	$Pd(PPh_3)_2Cl_2$	60
7	$Pd(PCy_3)_2Cl_2$	58
8	$Pd(PPh_3)_4$	67
9	$Pd(OAc)_2/PCy_3$	66
10	$Pd(OAc)_2$/dppf	68
11	$Pd(OAc)_2$/1,10-phenanthroline	0

[a] Reaction conditions: (*E*)-ethyl 3-phenoxyacrylate (1.0 mmol), Pd source (0.05 mmol), ligand if necessary (0.05 mmol), C_6H_6 (2.0 mL), CF_3CO_2Ag (2.0 mmol) at 110 °C, under air, 24 h. [b] Isolated yields.

Table 3. $Pd(OAc)_2$-Catalyzed Cyclization Reactions[a]



1 2

entry	R^1	R^2	2	yield (%)[b]
1	H	Et	**2a**	81
2	4-Me	Et	**2b**	85
3	3-Me	Et	**2c**	79
4	2-Me	Et	**2d**	73
5	4-OMe	Et	**2e**	72
6	4-Cl	Et	**2f**	64
7	2-Cl	Et	**2g**	58
8	2,4-Cl_2	Et	**2h**	51
9	4-*t*-Bu	Et	**2i**	82
10	2-Ph	Et	**2j**	75
11	2,4-$(Me)_2$	Et	**2k**	74
12	2,3-$(Me)_2$	Et	**2l**	78
13			**2m**	82
14	H	Me	**2n**	75
15	4-Me	Me	**2o**	81
16	3-Me	Me	**2p**	80
17	2-Me	Me	**2q**	75

[a] Reaction conditions: (*E*)-3-phenoxyacrylate (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.05 mmol), CF_3CO_2Ag (2.0 mmol), C_6H_6 (2.0 mL) at 110 °C, under air, 24 h. [b] Isolated yields.

electron-withdrawing groups attached to the benzene rings, were able to undergo cyclization reaction smoothly and generated the corresponding products in good yields (Table 3, entries 1−12). It is important to note that the palladium-catalyzed cyclization

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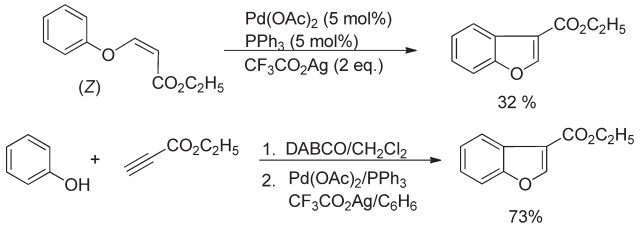
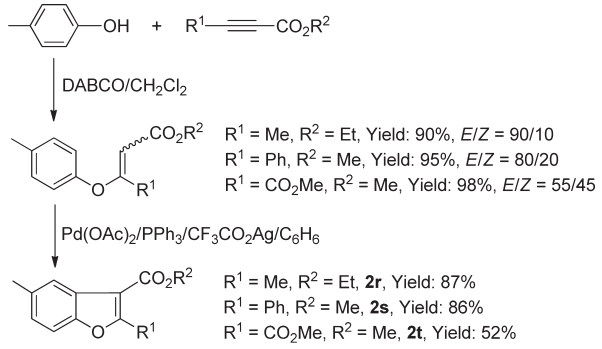
Scheme 1



Scheme 2

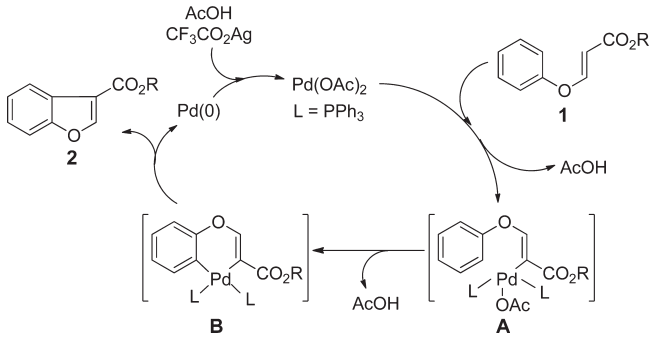


reaction could tolerate *ortho*-substituted substrates, and the corresponding products were obtained in moderate to good yields (Table 3, entries 4, 7, 8, and 10−12). Fortunately, a substrate derived from α-naphthalenol and ethyl propiolate displayed high reactivity under the optimized reaction conditions and generated the desired products in 82% yield (Table 3, entry 13). In order to expand the scope of propiolate, (*E*)-methyl 3-phenoxyacrylate derived from phenol or substituted phenol and methyl propiolate were also surveyed. The results showed that good yields of the corresponding products were isolated (Table 3, entries 14−17). It should be noted that the cyclization products in entries 3 and 16 were 6-methylbenzofuran-3-carboxylates (**2c** and **2p**).

In general, a mixture of a pair of *Z*- and *E*-isomers was obtained from the reaction of phenols and propiolates. We subsequently investigated (*Z*)-ethyl 3-phenoxyacrylate, which was prepared according to the literature, as a starting material to undergo the oxidative cyclization reaction under the recommended reaction conditions. Only 32% yield of the desired product was isolated, and starting material was recovery in 65% yield (Scheme 1). (*Z*)-Ethyl 3-phenoxyacrylate could be converted into its (*E*)-isomer in 20% yield in benzene at 110 °C for 2 h.[13] It is evident that (*E*)-isomer favors the reaction, and (*Z*)-isomer disfavors the reaction. In addition, a one-pot sequence reaction enables rapid access to benzofurans from commercially available phenols and propiolates. Phenol was reacted with ethyl propiolate at room temperature in the presence of DABCO in CH_2Cl_2 for 15 min to give the corresponding ethyl 3-phenoxyacrylate, which underwent subsequent oxidative cyclization under the standard reaction conditions with additional HAc (0.2 equiv) to give the desired product **2a** in 73% yield (Scheme 1).

We further investigated the substrates derived from 4-methylphenol with ethyl but-2-ynoate, ethyl 3-phenylpropiolate, and dimethyl acetylenedicarboxylate (Scheme 2). The substrates were prepared from the reaction of 4-methylphenol with various

Scheme 3. Plausible Mechanism



3-substituted propiolates catalyzed by DABCO in CH_2Cl_2 for 15 min at room temperature in excellent yields. The ^{1}H NMR analysis of the product showed that the corresponding product as a pair of *Z*- and *E*-isomers was obtained with ratios of *E*/*Z* in the range of 90/10 to 55/45.[12] We were also pleased to find that the obtained substrates underwent palladium-catalyzed oxidative cyclization smoothly to give the corresponding substituted benzofurans in moderate to good yields (Scheme 2). The isolated yields of benzofurans with an electron-donating group at the 2-position were much better than those of benzofurans with an electron-withdrawing group at the 2-position. This may be attributed to the *E*/*Z* ratios of substrates and electronic factors of the substituted groups.

A plausible mechanism of the palladium-catalyzed intramolecular oxidative cyclization of 3-phenoxyacrylates was proposed in Scheme 3. The reaction occurs probably involving (1) the formation of a vinylpalladium intermediate **A** by the electrophilic palladation of **1** with $Pd(OAc)_2$ through C−H activation of the vinyl proton with the assistance of PPh_3 as ligand and deprotonation,[14,11b,11d] (2) the intramolecular electrophilic aromatic palladation of **A** through C−H activation of the aromatic hydrogen and subsequent proton abstraction,[15] forming an intermediate **B**, (3) the carbon−carbon bond formation via reductive elimination of **B**, affording the corresponding benzofuran product **2** and palladium(0), and finally, (4) the oxidation of Pd^0 by the oxidant CF_3CO_2Ag, regenerating the Pd^{II} species to complete this catalytic cycle. It should be noted that the oxidative cyclization was suppressed by additional base, such as K_2CO_3 or Et_3N in a dose-dependent manner.

In conclusion, we have developed an efficient and applicable method for the synthesis of benzofurans from commercially available phenols and propiolate. The process was simple, and a diverse range of benzofurans were generated in good yields. Moreover, this transformation of phenols into benzofurans can also be carried out in one pot. The method is an attractive alternative to Heck and Sonagashira coupling reactions, which require the use of *ortho*-halogen-substituted phenols.

EXPERIMENTAL SECTION

General Procedure for the Palladium-Catalyzed Cyclization Reactions. Under air atmosphere, a sealable reaction tube with a Teflon-coated screw cap equipped with a magnetic stir bar was charged with (*E*)-3-phenoxyacrylate (1.0 mmol), $Pd(OAc)_2$ (11.3 mg, 0.05 mmol), PPh_3 (13.1 mg, 0.05 mmol), CF_3CO_2Ag (440 mg, 2.0 mmol), and C_6H_6 (2.0 mL). The reaction vessel was placed in an oil bath at

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110 °C, and the mixture was stirred for 24 h and then cooled to room temperature. The solvent was filtered and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel (eluant: hexane/ethyl acetate) to give the corresponding cyclization reaction product.

Typical Procedure for the Synthesis of 2a in One Pot. A Schlenk tube with a magnetic stirring bar was charged with ethyl propiolate (1.0 mmol), phenol (1.0 mmol), DABCO (0.10 mmol), and CH_2Cl_2 (2.0 mL). The reaction mixture was stirred for 15 min at room temperature, and then the solvent was evaporated under reduced pressure. $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.05 mmol), CF_3CO_2Ag (2.0 mmol), HAc (0.20 mmol), and C_6H_6 (2.0 mL) was added to the above Schlenk tube. The reaction vessel was placed in an oil bath at 110 °C, and the mixture was stirred for 24 h, then it was cooled to room temperature. The solvent was filtered and concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel to give **2a** (138 mg, 73% yield).

Cyclization compounds, ethyl benzofuran-3-carboxylate (**2a**),[16] methyl benzofuran-3-carboxylate (**2n**),[17] methyl 5-methylbenzofuran-3-carboxylate (**2o**),[17] and methyl 6-methylbenzofuran-3-carboxylate (**2p**)[17] have been previously reported, and their identities were confirmed by comparison of their spectral data with reported ones.

Ethyl 5-methylbenzofuran-3-carboxylate (2b): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.20 (s, 1H), 7.85 (s, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.16−7.13 (m, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.47 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 154.0, 151.0, 133.7, 126.4, 124.6, 121.7, 114.3, 111.0, 60.4, 21.3, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{12}H_{12}O_3$ 204.0786, found 204.0784.

Ethyl 6-methylbenzofuran-3-carboxylate (2c): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.18 (s, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.31 (s, 1H), 7.16 (d, J = 8.0 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.47 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 156.0, 150.3, 135.5, 125.5, 122.0, 121.4, 114.5, 111.7, 60.4, 21.6, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{12}H_{12}O_3$ 204.0786, found 204.0783.

Ethyl 7-methylbenzofuran-3-carboxylate (2d): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.24 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 8.0 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.51 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 154.6, 150.6, 126.0, 124.1, 121.8, 119.3, 114.8, 60.4, 14.8, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{12}H_{12}O_3$ 204.0786, found 204.0785.

Ethyl 5-methoxybenzofuran-3-carboxylate (2e): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21 (s, 1H), 7.52 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 4.41 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 156.9, 151.4, 150.5, 125.4, 114.6, 114.4, 112.2, 103.7, 60.4, 55.8, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{12}H_{12}O_4$ 220.0736, found 220.0733.

Ethyl 5-chlorobenzofuran-3-carboxylate (2f): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.26 (s, 1H), 8.03 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.34−7.31 (m, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.9, 153.9, 152.0, 130.0, 126.0, 125.6, 121.8, 114.5, 112.7, 60.8, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{11}H_9O_3Cl$ 224.0240, found 224.0236.

Ethyl 7-chlorobenzofuran-3-carboxylate (2g): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.29 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.30 (m, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.8, 151.3, 130.9, 126.3, 125.4, 125.0, 120.6, 117.1, 115.4, 60.8, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{11}H_9O_3Cl$ 224.0240, found 224.0238.

Ethyl 5,7-dichlorobenzofuran-3-carboxylate (2h): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.30 (s, 1H), 7.94 (d, J = 1.6 Hz, 1H), 7.37 (d, J = 1.6 Hz, 1H), 4.42 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.3, 152.2, 149.9, 130.3, 127.0, 125.6, 120.4, 117.7, 115.2, 61.0, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{11}H_8O_3Cl_2$ 257.9850, found 257.9848.

Ethyl 5-*tert*-butylbenzofuran-3-carboxylate (2i): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.23 (s, 1H), 8.10 (s, 1H), 7.47−7.42 (m, 2H), 4.42 (q, J = 7.2 Hz, 2H), 1.44 (t, J = 7.2 Hz, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.6, 153.8, 151.0, 147.3, 124.3, 123.2, 118.0, 114.6, 110.9, 60.4, 34.8, 31.8, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{15}H_{18}O_3$ 246.1256, found 246.1257.

Ethyl 7-phenylbenzofuran-3-carboxylate (2j): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.32 (s, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.54−7.50 (m, 3H), 7.47−7.42 (m, 2H), 4.45 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.4, 152.8, 150.9, 135.7, 128.6, 127.9, 125.9, 125.3, 124.8, 124.7, 121.1, 114.8, 60.6, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{17}H_{14}O_3$ 266.0943, found 226.0940.

Ethyl 5,7-dimethylbenzofuran-3-carboxylate (2k): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.21 (s, 1H), 7.66 (s, 1H), 6.97 (s, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.48 (s, 3H), 2.44 (s, 3H), 1.42 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.7, 153.2, 150.8, 133.8, 127.5, 124.2, 121.2, 119.0, 114.5, 60.4, 21.3, 14.8, 14.4; HRMS (ESI) ($[M]^+$) calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0936.

Ethyl 6,7-dimethylbenzofuran-3-carboxylate (2l): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.19 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.14 (d, J = 8.0 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.42 (s, 3H), 2.38 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.7, 155.2, 150.2, 133.7, 126.2, 121.9, 120.1, 118.4, 114.9, 60.4, 19.1, 14.3, 11.5; HRMS (ESI) ($[M]^+$) calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0945.

Ethyl naphtho[1,2-b]furan-3-carboxylate (2m): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.32 (s, 1H), 8.25 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.60−7.56 (m, 1H), 7.52−7.48 (m, 1H), 4.42 (q, J = 8.0 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 151.2, 149.6, 131.7, 128.3, 126.6, 125.7, 124.7, 121.0, 120.6, 119.8, 119.6, 115.7, 60.5, 14.3; HRMS (ESI) ($[M]^+$) calcd for $C_{15}H_{12}O_3$ 240.0786, found 24.0788.

Methyl 7-methylbenzofuran-3-carboxylate (2q): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.25 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 7.2 Hz, 1H), 7.15 (d, J = 7.2 Hz, 1H), 3.94 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.8, 154.6, 150.6, 126.0, 124.1, 124.0, 121.8, 119.3, 114.5, 51.4, 14.7; HRMS (ESI) ($[M]^+$) calcd for $C_{11}H_{10}O_3$ 190.0630, found 190.0629.

Ethyl 2,5-dimethylbenzofuran-3-carboxylate (2r): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.74 (s, 1H), 7.28 (d, J = 8.4 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 2.73 (s, 3H), 2.45 (s, 3H), 1.44 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.6, 151.9, 133.1, 126.2, 125.3, 121.5, 114.5, 110.1, 108.6, 60.1, 21.4, 14.5, 14.4; HRMS (ESI) ($[M]^+$) calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0945.

Methyl 5-methyl-2-phenylbenzofuran-3-carboxylate (2s): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.97 (d, J = 6.4 Hz, 2H), 7.77 (s, 1H), 7.41−7.39 (m, 3H), 7.29 (d, J = 8.4 Hz, 1H), 7.05 (d, J = 8.4 Hz, 1H), 3.84 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.2, 160.5, 151.9, 133.2, 129.9, 129.4, 129.1, 127.7, 126.7, 126.2, 122.1, 110.3, 108.1, 51.2, 21.2; HRMS (ESI) ($[M]^+$) calcd for $C_{17}H_{14}O_3$ 266.0943, found 266.0940.

Dimethyl 5-methylbenzofuran-2,3-dicarboxylate (2t): ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.65 (s, 1H), 7.42 (d, J = 8.8 Hz, 1H), 7.26 (t, J = 8.8 Hz, 1H), 3.99 (s, 3H), 3.98 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.0, 159.1, 152.6, 145.4, 134.6, 129.7, 125.4, 122.2, 118.0, 111.7, 52.9, 52.5, 21.4; HRMS (ESI) ($[M]^+$) calcd for $C_{13}H_{12}O_5$ 248.0685, found 248.0683.

■ ASSOCIATED CONTENT

Supporting Information. Copies of ^{1}H and ^{13}C NMR spectra of all cyclization products. This material is available free of charge via the Internet at http://pubs.acs.org.

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