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Palladium-Catalyzed Synthesis of 2,3,4-Trisubstituted Furans via Cascade Reactions of Aryloxy-enynes with Aryl Halides

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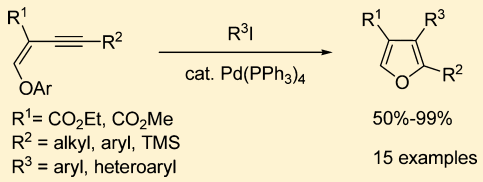
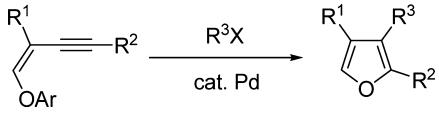
Supporting Information

ABSTRACT: A highly efficient palladium-catalyzed cascade reactions of aryloxy-enynes with aryl halides under mild reaction conditions has been developed. This methodology offers rapid access to 2,3,4-trisubstituted furans in good to excellent yields in a regioselective manner.



Substituted furans are important structural units which are found in many biologically active natural and artificial compounds.[1,2] They are also versatile building blocks in synthetic organic chemistry.[3] As a consequence, a variety of synthetic routes toward furan ring formation have been disclosed,[4] the majority of which include the classical approaches, such as Paal–Knorr synthesis,[5] Feist–Benary method,[6] and O-annulation reactions from acyclic starting materials. Among the many approaches to substituted furans, the intramolecular attack of a nucleophilic oxygen atom onto a C–C triple bond offers a straightforward access to furan derivatives either by the electrophilic cyclization of functionally substituted alkynes or the transition-metal-catalyzed cyclization. The acyclic precursors involve allenyl ketones,[7] alkynyl ketones,[8] 2-(1-alkynyl)-2-alken-1-ones,[9] enynols or phenols,[10] 1,3-enynyl ketones,[11] and others.[12] Although these methods are efficient for the substituted furan formation, the development of synthetic procedures that allow the facile assembly of substituted furans from readily available starting materials still remains an important task in organic chemistry. Recently, we reported a Au-catalyzed methodology for the preparation of 2,4-disubstituted furans from aryloxy-enynes.[13] We envisioned that one more substituent might be introduced to the C-3 position of the furan ring from the same starting materials by the proper choice of metal catalyst, such as palladium catalyst, and resulting in the trisubstituted furans. It is well-known that Pd(II) species are efficient catalysts for the C–C triple bond activation,[14] and it can be generated conveniently from Pd(0) and aryl halide (Scheme 1). Herein, we would like to report the effective synthesis of 2,3,4-trisubstituted furans through the Pd-catalyzed cascade reactions of aryloxy-enyne and aryl halides.

Scheme 1



The requisite (*E*)-1-aryloxy-1-en-3-ynes with an ester group on C-2 (**1**) were synthesized via the Sonogashira coupling of the corresponding 2-bromo-3-aryloxypropenoates and terminal alkynes.[13] First, the reaction of (*E*)-1-phenoxy-1-en-3-yne with an ethyl ester group on C-2 (**1a**) with ethyl 4-iodobenzoate (**2a**) was carried out using $PdCl_2(PPh_3)_2$ (5 mol %) as the catalyst and Cs_2CO_3 (2 equiv) as the base in dioxane at 70 °C. However, the desired furan **3a** was produced in only 35% yield after 6 h (Table 1, entry 1). When the catalyst was changed to $Pd(PPh_3)_4$, the yield of **3a** increased to 66% (Table 1, entry 3). It is interesting that $PdCl_2(PPh_3)_2$ combined with DMF afforded **3a** in 87% yield within 2 h (Table 1, entry 2). It seems that DMF is better than dioxane, and Pd(0) is more efficient than Pd(II) in our system. Then the combination of $Pd(PPh_3)_4$ and DMF was tested; satisfyingly, the desired trisubstituted furan was produced quantitatively (Table 1, entry 4). Lowering the catalyst loading to 2 mol % gave 75% yield (Table 1, entry 5). When the reaction was carried out at 40 °C, no desired product could be detected (Table 1, entry 8). $Pd_2(dba)_3$ resulted in moderate yield of the desired furan (Table 1, entry 17). When **2a** was reduced to 1.0 equiv, the yield of **3a** was decreased to 83% (Table 1, entry 7). Changing the solvent to THF, toluene, DMA (*N*,*N*-dimethylacetamide), or DMSO, **3a** was produced in relatively lower yields (Table 1, entries 9–12). The use of other bases such as K_2CO_3, Na_2CO_3, NaOAc, or K_3PO_4 gave no better results than that of Cs_2CO_3 (Table 1, entries 13–16). Therefore, the optimized reaction condition was to use 5 mol % of $Pd(PPh_3)_4$ as the catalyst, 2.0 equiv of Cs_2CO_3 as the base, and DMF as the solvent at 70 °C. One of the advantages of this method to furans is that the regioselective introduction of substituents on the furan ring comes down to the appropriate choice of the aryloxy-enyne and aryl halide, which allows for considerable versatility.

With the optimized reaction conditions in hand, we next examined the substrate scope of this catalytic method for the

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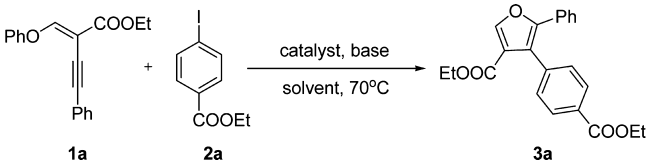
Table 1. Optimization of Reaction Conditions for the Formation of 3a



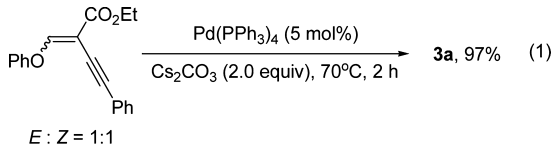
1a **2a** **3a**

entry	catalyst	base (n equiv)	solvent	time (h)	yield[a,b] (%)
1	$PdCl_2(PPh_3)_2$	Cs_2CO_3 (2.0)	dioxane	6	35
2	$PdCl_2(PPh_3)_2$	Cs_2CO_3 (2.0)	DMF	2	87
3	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	dioxane	12	66
4	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	DMF	1.5	99
5	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	DMF	2	75[c]
6	$Pd(PPh_3)_4$	Cs_2CO_3(1.0)	DMF	2	26
7	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	DMF	2	83[d]
8	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	DMF	6	[e]
9	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	THF	12	86
10	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	Tol	12	50
11	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	DMA	1.5	91
12	$Pd(PPh_3)_4$	Cs_2CO_3 (2.0)	DMSO	1.5	80
13	$Pd(PPh_3)_4$	K_2CO_3 (2.0)	DMF	19	70
14	$Pd(PPh_3)_4$	Na_2CO_3 (2.0)	DMF	24	12
15	$Pd(PPh_3)_4$	NaOAc (2.0)	DMF	24	50
16	$Pd(PPh_3)_4$	K_3PO_4 (2.0)	DMF	7	74
17	$Pd_2(dba)_3$	Cs_2CO_3 (2.0)	DMF	2	59

[a]Unless otherwise noted, all reactions were carried out using 5 mol % of catalyst with the ratio of **1a**/**2a** = 1:1.5. [b]Isolated yield. [c]2 mol % of Pd catalyst was used. [d]Ratio of **1a**/**2a** = 1:1. [e]Reaction was carried out at 40 °C.

synthesis of 2,3,4-trisubstituted furans using a variety of (*E*)-1-aryloxy-1-en-3-ynes and aryl iodides, and the results are shown in Table 2. We first investigated the electronic effects of the aromatic substituents on the triple bond. It was found that electron-donating aryl groups such as −Me (**1b**) or −2,3,4-trimethoxyl (**1c**) reacted with 4-iodobenzoate (**2a**) to afford the corresponding products **3b** and **3c** in 82 and 91% yields, respectively (Table 2, entries 1 and 2). An electron-withdrawing (−Cl) aryl group afforded the corresponding furan **3d** in 78% yield (Table 2, entry 3). Naphthyl-substituted **1e** gave a good result (Table 2, entry 4). The substituents on the triple bond could also be alkyl groups, such as *n*-butyl (**1f**), *n*-pentyl (**1g**), and phenylethyl (**1h**), furnishing **3f**, **3g**, and **3h** in 66, 72, and 50% yields, respectively (Table 2, entries 5−7). Enynyl ether **1a** reacted smoothly with iodobenzene (**2b**) to give **3i** in 92% yield (Table 2, entry 8). The aryl iodides could also be 4-methyl (**2c**) or 4-nitroiodobenzene (**2d**), and the corresponding furans were produced in 87% (**3j**) and 82% (**3k**) yields, respectively (Table 2, entries 9 and 10). The structure of **3k** was further confirmed by X-ray crystallographic analysis. 2-Bromo-1-iodobenzene could also be employed in the reaction, providing the desired **3l** in good yield, and the −Br group was well-tolerated during the reaction (Table 2, entry 11). Heteroaryl idodide such as 2-iodothiophene (**2f**) led to the formation of **3m** in 64% yield (Table 2, entry 12). When the ester group of enynyl ether was methyl ester, the corresponding furan **3n** was produced in 57% yield (Table 2, entry 13). It is worthy to note when the trimethylsilyl-substituted enynyl ether **1j** was used to react with 2.5 equiv of iodobenzene, **3i** was obtained in 63% yield. It might due to the further desilylation coupling of the initially formed C-3 TMS-substituted furan with iodobenzene catalyzed by the Pd catalyst (Table 2, entry 14).

Very interestingly, a mixture of **1a** (*E*/*Z* = 1:1) could also afford the desired **3a** in high yield under the optimal conditions (eq 1). This result may further broaden the substrate scope of this method.



According to our previous results, one possibility of the reaction pathway is that the enynyl ether **1** is hydrolyzed to the corresponding carbonyl group by H_2O, and then undergo an O-cyclization.[13] To prove this point, we carried out an isotopic labeling experiment using **1a** and **2a** with 3 equiv of $H_2{}^{18}O$ and found that 43% of ^{18}O was incorporated in the final furan ring; the desired furan was obtained in 97% yield in 3 h (Scheme 2).

On the basis of the above observations and the reported work, a possible reaction mechanism is proposed in Scheme 3. First, oxidative addition of aryl iodide to Pd(0) gives Pd(II), which may act as a Lewis acid[12j,14] to activate the enone moiety of compound **1**, then nucleophilic attack of H_2O to the C−C double bond followed by elimination of PhOH gives intermediate **5** or **6**. Then **6** is activated by the coordination of the alkynyl moiety to Pd(II) which enhances the electrophilicity of the triple bond and facilitates an intramolecular cyclization of the enol oxygen onto the alkyne to afford **8**. Reductive elimination of **8** with regeneration of the Pd(0) catalyst furnishes the desired furan **3**.

In conclusion, we have shown that 2,3,4-trisubstituted furans can be efficiently prepared by the Pd-catalyzed cascade reactions using aryloxy-enynes and aryl iodides. Aryl, alkyl, and trimethylsilyl substituents on the acetylene terminus are compatible in the annulation reaction, furnishing the desired furans in good to high yields. In this procedure, the regioselective introduction of substituents on the furan ring comes down to the appropriate choice of the aryloxy-enyne and aryl halide, which allows for considerable versatility.

EXPERIMENTAL SECTION

Typical Procedure for the Pd-Catalyzed Formation of Ethyl 4-(4-(Ethoxycarbonyl)phenyl)-5-phenylfuran-3-carboxylate (3a). $Pd(PPh_3)_4$ (12 mg, 0.01 mmol), (*E*)-ethyl-2-(phenoxymethylene)-4-phenylbut-3-ynoate (58 mg, 0.2 mmol) in DMF (2 mL), ethyl 4-iodobenzoate (0.05 mL, 0.3 mmol), and Cs_2CO_3 (130 mg, 0.4 mmol) were added to a Schlenk tube under nitrogen. The resulting solution was stirred at 70 °C. After the reaction was complete as monitored by thin-layer chromatography, the mixture was treated with water and extracted with EA. The extract was washed with water and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure, and the residue was purified by chromatography on silica gel to afford the 2,3,4-trisubstituted furan derivative **3a** (72 mg, 99%) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.17 (t, J = 7.2 Hz, 3H), 1.41 (t, J = 7.2 Hz, 3H), 4.17 (q, J = 7.2 Hz, 2H), 4.41 (q, J = 7.2 Hz, 2H), 7.22−7.26 (m, 3H), 7.32−7.34 (m, 2H), 7.42−7.44 (m, 2H), 8.07−8.09 (m, 2H), 8.13 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 14.3, 60.3, 60.9, 120.4, 120.5, 125.9, 128.1, 128.4, 129.4, 129.6, 129.7, 130.4, 137.4, 147.3, 150.9, 162.6, 166.5; HRMS (EI) calcd for $C_{22}H_{20}O_5$ 364.1311, found 364.1312.

Ethyl 4-(4-(Ethoxycarbonyl)phenyl)-5-*p*-tolylfuran-3-carboxylate (3b). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3b** in 82% isolated yield as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.17 (t, J = 6.8

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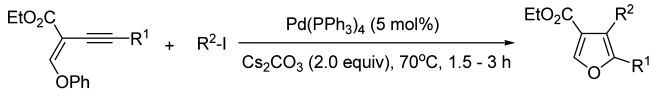
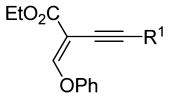
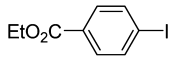
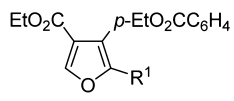
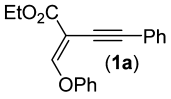
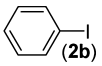
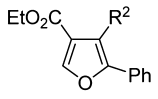
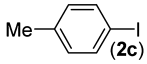
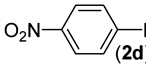
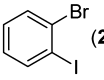
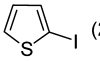
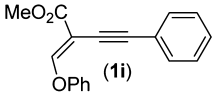
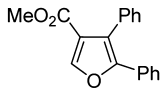
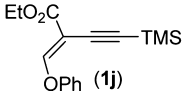
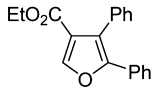
Table 2. Synthesis of Various of 2,3,4-Trisubstituted Furans

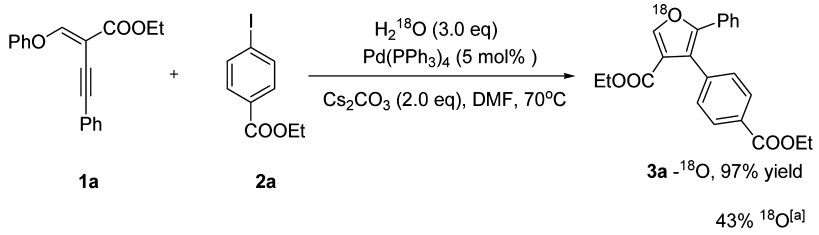


1 2 3

entry	enynyl ether	aryl iodide	product		yield[a]
		 (**2a**)			
1	R^1 = *p*-MeC_6H_4 : **1b**	**2a**	R^1 = *p*-MeC_6H_4	**3b**	82%
2	R^1 = 3,4,5-tri$MeOC_6H_4$: **1c**	**2a**	R^1 = 3,4,5-tri$MeOC_6H_4$	**3c**	91%
3	R^1 = *p*-ClC_6H_4 : **1d**	**2a**	R^1 = *p*-ClC_6H_4	**3d**	78%
4	R^1 = 1-Naphthyl : **1e**	**2a**	R^1 = 1-Naphthyl	**3e**	60%
5	R^1 = *n*-Butyl : **1f**	**2a**	R^1 = *n*-Butyl	**3f**	66%[b]
6	R^1 = *n*-Pentyl : **1g**	**2a**	R^1 = *n*-Pentyl	**3g**	72%[b]
7	R^1 = Phenylethyl : **1h**	**2a**	R^1 = Phenylethyl	**3h**	50%
8	 (**1a**)	 (**2b**)		**3i** R^2 = Ph	92%
9	**1a**	 (**2c**)	R^2 = *p*-MeC_6H_4	**3j**	87%
10	**1a**	 (**2d**)	R^2 = *p*-$NO_2C_6H_4$	**3k**	82%
11	**1a**	 (**2e**)	R^2 = *o*-BrC_6H_4	**3l**	78%
12	**1a**	 (**2f**)	R^2 = 2-thienyl	**3m**	64%
13	 (**1i**)	**2b**		**3n**	57%
14	 (**1j**)	**2b**		**3i**	63%[c]

[a]Isolated yields. Unless noted, all of the reactions were carried out using 5 mol % of $Pd(PPh_3)_4$ and 2.0 equiv of Cs_2CO_3 in DMF at 70 °C. [b]The reaction time was 12 h. [c]2.5 equiv of **2b** was used.

Scheme 2. Isotopic Experiment[a]



1a **2a**

3a -^{18}O, 97% yield

43% ^{18}O[a]

[a][a] Determined by MS.

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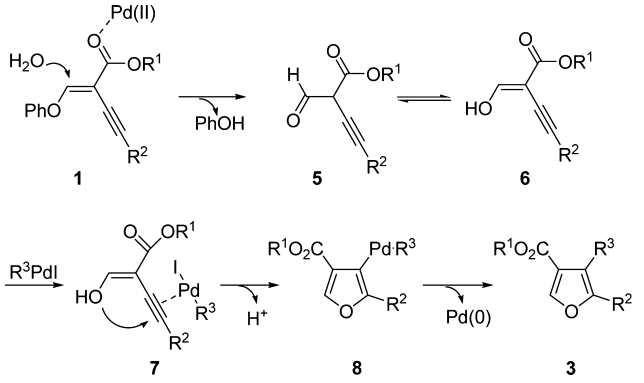
Scheme 3. Proposed Reaction Pathway



Hz, 3H), 1.41 (t, J = 6.8 Hz, 3H), 2.29 (s, 3H), 4.16 (q, J = 7.2 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 7.02−7.04 (m, 2H), 7.20−7.22 (m, 2H), 7.41−7.44 (m, 2H), 8.07−8.09 (m, 2H), 8.10 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 14.3, 21.1, 60.2, 60.9, 119.8, 120.3, 125.9, 126.8, 129.1, 129.4, 129.5, 130.4, 137.5, 138.1, 147.0, 151.2, 162.7, 166.5; HRMS (EI) calcd for $C_{23}H_{22}O_5$ 378.1467, found 378.1463.

Ethyl 4-(4-(Ethoxycarbonyl)phenyl)-5-(3,4,5-trimethoxyphenyl)furan-3-carboxy- late (3c). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3c** in 91% isolated yield as a light white crystalline solid: mp 105−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.18 (t, J = 6.9 Hz, 3H), 1.41 (t, J = 6.9 Hz, 3H), 3.61 (s, 6H), 3.82 (s, 3H), 4.17 (q, J = 7.2 Hz, 2H), 4.41 (q, J = 7.2 Hz, 2H), 6.58 (s, 2H), 7.46−7.49 (m, 2H), 8.11−8.13 (m, 2H), 8.13 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 13.9, 14.2, 55.6, 60.2, 60.7, 60.9, 103.0, 120.1, 120.5, 124.9, 129.4, 129.6, 130.4, 137.7, 137.8, 146.8, 150.6, 153.0, 162.5, 166.2; HRMS (EI) calcd for $C_{25}H_{26}O_8$ 454.1628, found 454.1626.

Ethyl 5-(4-Chlorophenyl)-4-(4-(ethoxycarbonyl)phenyl)-furan-3-carboxylate (3d). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3d** in 78% isolated yield as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.17 (t, J = 7.2 Hz, 3H), 1.41 (t, J = 7.2 Hz, 3H), 4.17 (q, J = 6.8 Hz, 2H), 4.41 (q, J = 6.8 Hz, 2H), 7.18−7.21 (m, 2H), 7.24−7.26 (m, 2H), 7.40−7.43 (m, 2H), 8.08−8.10 (m, 2H), 8.12 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 14.3, 60.3, 61.0, 120.6, 121.0, 127.1, 128.1, 128.7, 129.5, 129.9, 130.2, 134.0, 137.0, 147.4, 149.8, 162.4, 166.3; HRMS (EI) calcd for $C_{22}H_{19}O_5Cl$ 398.0921, found 398.0922.

Ethyl 4-(4-(Ethoxycarbonyl)phenyl)-5-(naphthalen-1-yl)-furan-3-carboxylate (3e). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3e** in 60% isolated yield as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.26 (t, J = 6.8 Hz, 3H), 1.33 (t, J = 6.8 Hz, 3H), 4.26 (q, J = 7.2 Hz, 2H), 4.31 (q, J = 6.8 Hz, 2H), 7.26−7.33 (m, 4H), 7.43−7.48 (m, 2H), 7.82−7.88 (m, 5H), 8.29 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$, Me_4Si) δ 14.0, 14.2, 60.4, 60.8, 119.3, 123.1, 125.0, 125.4, 126.1, 126.7, 126.8, 128.4, 128.9, 129.1, 129.3, 129.8, 130.2, 131.8, 133.6, 136.4, 148.4, 152.0, 162.8, 166.4; HRMS (EI) calcd for $C_{26}H_{22}O_5$ 414.1467, found 414.1463.

Ethyl 5-Butyl-4-(4-(ethoxycarbonyl)phenyl)furan-3-carboxylate (3f). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3f** in 66% isolated yield as a light white oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 0.84 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 1.24−1.30 (m, 2H), 1.40 (t, J = 7.2 Hz, 3H), 1.57−1.61 (m, 2H), 2.58 (t, J = 7.2 Hz, 2H), 4.17 (q, J = 6.8 Hz, 2H), 4.39 (q, J = 7.2 Hz, 2H), 7.36−7.38 (m, 2H), 7.98 (s, 1H), 8.06−8.08 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 13.6, 14.1, 14.3, 22.1, 25.8, 30.3, 60.1, 60.9, 118.6, 120.0, 129.0, 129.1, 130.1, 137.1, 146.8, 155.0, 163.0, 166.5; HRMS (EI) calcd for $C_{20}H_{24}O_5$ 344.1624, found 344.1627.

Ethyl 4-(4-(Ethoxycarbonyl)phenyl)-5-pentylfuran-3-carboxylate (3g). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3g** in 72% isolated yield as a light white oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 0.84 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H), 1.22−1.26 (m, 4H), 1.40 (t, J = 7.2 Hz, 3H), 1.59−1.62 (m, 2H), 2.57 (t, J = 7.2 Hz, 2H), 4.17 (q, J = 6.8 Hz, 2H), 4.40 (q, J = 7.2 Hz, 2H), 7.36−7.38 (m, 2H), 7.98 (s, 1H), 8.06−8.08 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 13.8, 14.1, 14.3, 22.2, 26.0, 27.9, 31.1, 60.1, 60.8, 118.6, 120.0, 129.0, 129.1, 130.0, 137.1, 146.8, 155.1, 163.0, 166.5; HRMS (EI) calcd for $C_{21}H_{26}O_5$ 358.1780, found 358.1776.

Ethyl 4-(4-(Ethoxycarbonyl)phenyl)-5-phenethylfuran-3-carboxylate (3h). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3h** in 50% isolated yield as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.17 (t, J = 7.2 Hz, 3H), 1.39 (t, J = 6.8 Hz, 3H), 2.83−2.87 (m, 2H), 2.91−2.94 (m, 2H), 4.15 (q, J = 6.8 Hz, 2H), 4.38 (q, J = 7.6 Hz, 2H), 6.99−7.01 (m, 2H), 7.05−7.08 (m, 2H), 7.18−7.25 (m, 3H), 7.95−7.98 (m, 2H), 8.01 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 14.3, 28.2, 34.3, 60.2, 60.9, 118.7, 121.0, 126.2, 128.3, 128.4, 128.9, 129.1, 130.0, 136.7, 140.3, 147.0, 153.5, 162.9, 166.5; HRMS (EI) calcd for $C_{24}H_{24}O_5$ 392.1624, found 392.1620.

Ethyl 4,5-Diphenylfuran-3-carboxylate (3i). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3i** in 92% isolated yield as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.15 (t, J = 7.2 Hz, 3H), 4.15 (q, J = 6.8 Hz, 2H), 7.20−7.22 (m, 3H), 7.33−7.40 (m, 7H), 8.10 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 60.1, 120.7, 121.5, 125.8, 127.6, 127.8, 128.2, 128.3, 130.1, 130.2, 132.4, 147.0, 150.6, 162.8; HRMS (EI) calcd for $C_{19}H_{16}O_3$ 292.1099, found 292.1098.

Ethyl 5-Phenyl-4-p-tolylfuran-3-carboxylate (3j). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3j** in 87% isolated yield as a light yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 1.18 (t, J = 6.8 Hz, 3H), 2.39 (s, 3H), 4.17 (q, J = 7.2 Hz, 2H), 7.18−7.24 (m, 7H), 7.37−7.40 (m, 2H), 8.08 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 21.3, 60.1, 120.7, 121.6, 125.7, 127.9, 128.3, 129.0, 129.2, 130.0, 130.2, 137.2, 146.9, 150.5, 162.8; HRMS (EI) calcd for $C_{20}H_{18}O_3$ 306.1256, found 306.1255.

Ethyl 4-(4-Nitrophenyl)-5-phenylfuran-3-carboxylate (3k). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3k** in 82% isolated yield as a yellow crystalline solid: mp 119−121 °C; ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.21 (t, J = 7.2 Hz, 3H), 4.20 (q, J = 7.2 Hz, 2H), 7.26−7.31 (m, 5H), 7.53−7.55 (m, 2H), 8.16 (s, 1H), 8.24−8.27 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.1, 60.5, 119.4, 120.1, 123.4, 126.2, 128.6, 128.6, 129.2, 131.5, 139.7, 147.3, 147.6, 151.4, 162.5; HRMS (EI) calcd for $C_{19}H_{15}NO_5$ 337.0950, found 337.0948.

Ethyl 4-(2-Bromophenyl)-5-phenylfuran-3-carboxylate (3l). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3l** in 78% isolated yield as a yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.11 (t, J = 6.9 Hz, 3H), 4.13 (q, J = 7.5 Hz, 2H), 7.22−7.36 (m, 8H), 7.68−7.71 (m, 1H), 8.14 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$, Me_4Si) δ 13.8, 60.2, 120.3, 121.0, 125.2, 127.4, 128.0, 128.5, 129.4, 129.8, 131.6, 132.6, 134.2, 146.8, 150.6, 162.6; HRMS (EI) calcd for $C_{19}H_{15}O_3Br$ 370.0205, found 370.0204.

Ethyl 5-Phenyl-4-(thiophen-2-yl)furan-3-carboxylate (3m). Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3m** in 64% isolated yield as a light yellow solid: ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ 1.21 (t, J = 6.9 Hz, 3H), 4.20 (q, J = 6.9 Hz, 2H), 7.04−7.11 (m, 2H), 7.25−7.28 (m, 3H), 7.41−7.47 (m, 3H), 8.10 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 14.0, 60.2, 113.9, 121.3, 126.0, 126.7, 127.1, 128.2, 128.4, 128.5, 129.7, 132.4, 147.0, 152.2, 162.5; HRMS (EI) calcd for $C_{17}H_{14}O_3S$ 298.0664, found 298.0660.

Methyl 4,5-Diphenylfuran-3-carboxylate (3n).[14c] Column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate = 50:1) afforded the title product **3n** in 57% isolated yield as a light yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 3.71 (s, 3H), 7.21 −7.24

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(m, 2H), 7.35−7.41 (m, 8H), 8.10 (s, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$, Me_4Si) δ 51.2, 120.3, 121.6, 125.9, 127.8, 127.9, 128.4, 128.4, 130.1, 130.3, 132.3, 147.2, 150.8, 163.3; HRMS (EI) calcd for $C_{18}H_{14}O_3$ 278.0943, found 278.0948.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

NMR spectra for new products and X-ray crystallography of compound **3k**. 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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