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# Copper(I)-Catalyzed $A^3$-Coupling Based Reaction of Alkynes, Aldehydes, and Amines: An Efficient Approach to 2,5-Polysubstituted Dihydrofurans and 2,5-Disubstituted Furans

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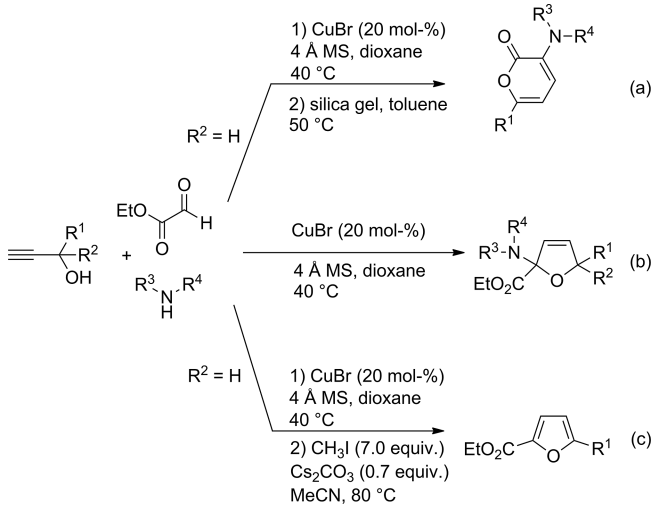
**Keywords:** Domino reactions / Multicomponent reactions / Oxygen heterocycles / Copper / Alkynes / Amines

An efficient and practical $A^3$-coupling based reaction that gives a variety of 2,5-polysubstituted dihydrofurans and 2,5-disubstituted furan derivatives has been developed. This domino copper-catalyzed three-component coupling reaction of propargylic alcohol, ethyl glyoxalate, and an amine affords a propargylic amine intermediate, which undergoes an alkyne–allene isomerization followed by a cyclization to yield the dihydrofuran. Upon treatment with $CH_3I$ and base, the latter was smoothly converted into a 2,5-disubstituted furan. Alternatively, the furan derivatives can be directly prepared by a two-step reaction sequence.

## Introduction

One goal of modern synthetic organic chemistry is the development of simple, convenient and efficient methods for the construction of target compounds from easily available starting materials. Multicomponent reactions, which allow the formation of several bonds including new C–C, C–O, and C–N bonds in one-pot, have emerged as an attractive and powerful strategy for this purpose. Of particular interest, copper-catalyzed $A^3$-coupling reactions of terminal alkynes, aldehydes, and amines have been well-developed.[1–3] Our group recently reported a unique copper-catalyzed three-component reaction for the synthesis of 3-amino-2-pyrones from secondary propargyl alcohols, ethyl glyoxalate, and amines (Scheme 1, a).[3j] A mechanistic investigation of this reaction indicated that a 2,5-dihydrofuran intermediate, which is formed by an $A^3$-coupling/alkyne–allene isomerization/cyclization process, was involved in the reaction pathway. We envision that by replacing the secondary propargyl alcohols with tertiary propargyl alcohols, the reaction would afford a five-membered 2,5-dihydrofuran as the only product. Herein, we report our investigation of copper(I)-catalyzed cascade three-component reactions for the formation of 2,5-dihydrofuran derivatives (Scheme 1, b). An efficient two-step sequence for the construction of functionalized 2,5-disubstituted furans from secondary propargyl alcohols, ethyl glyoxalate, and piperidine is also presented (Scheme 1, c).




Scheme 1. Previous work and this work (MS = molecular sieves).

## Results and Discussion

An initial study was performed by combining tertiary 2-methylbut-3-yn-2-ol (**1a**), piperidine (**2a**), and ethyl glyoxalate in 1,4-dioxane in the presence of a catalytic amount of CuBr at 40 °C, which produced the desired 2,5-dihydrofuran derivative **3aa** in 75% NMR yield (Table 1, Entry 1). A variety of copper salts were then studied, but no improvement to the yield was achieved (Table 1, Entries 2–6). Further solvent screening showed that ethereal solvents, such as tetrahydrofuran (THF) and 1,2-dimeth-

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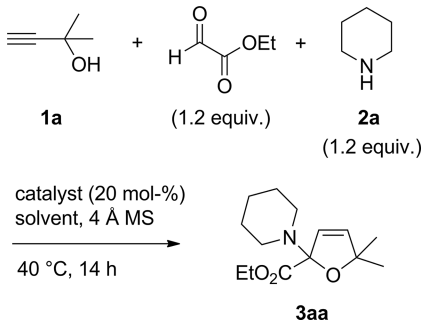
oxyethane (DME), gave similar results as dioxane (Table 1, Entries 7 and 8). Finally, the reaction conditions that are reported in Entry 1 of Table 1 were defined as the standard for further studies.

Table 1. Optimization of reaction conditions for preparing **3aa**.[a]




**3aa**

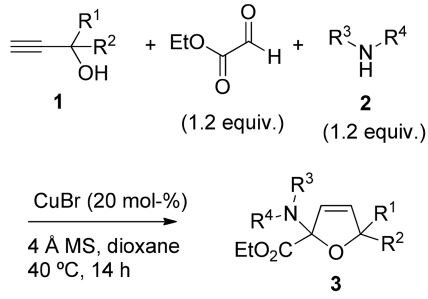
| Entry | Catalyst | Solvent | % Yield **3aa**[b] |
|---|---|---|---|
| 1 | CuBr | dioxane | 75 |
| 2 | CuI | dioxane | 51 |
| 3 | CuCl | dioxane | 72 |
| 4 | $CuBr_2$ | dioxane | 65 |
| 5 | $CuCl_2$ | dioxane | 66 |
| 6 | $Cu(OTf)_2$[c] | dioxane | 5 |
| 7 | CuBr | THF | 74 |
| 8 | CuBr | DME | 73 |
| 9 | CuBr | toluene | 61 |
| 10 | CuBr | DCM[c] | 64 |
| 11 | CuBr | $CH_3CN$ | 65 |

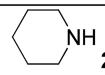
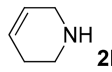
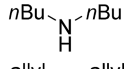
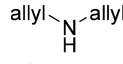
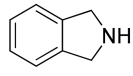
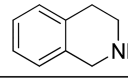
[a] Reagents and conditions: **1a** (1.0 mmol), ethyl glyoxalate (1.2 mmol), **2a** (1.2 mmol), MS (4 Å, 300 mg), and a copper salt (0.2 mmol) in solvent (3 mL) at 40 °C. [b] NMR yield. [c] Tf = trifluoromethylsulfonyl, DCM = dichloromethane.

With the optimized protocol in hand, we examined the scope of this three-component reaction (Table 2). A variety of different tertiary propargylic alcohols were compatible under the conditions and afforded the expected 2,5-dihydrofuran derivatives in good yields (Table 2, Entries 1–6). To our surprise, a five-membered 2,5-dihydrofuran ring could also be obtained by employing secondary propargylic alcohols (Table 2, Entries 7, 9, and 10). The employment of cyclic amines such as 1,2,3,6-tetrahydropyridine, pyrrolidine, and 3-pyrroline provided the desired products in decent yields (Table 2, Entries 11–13). Dibutyl and diallylamines were found to be similarly effective (Table 2, Entries 14 and 15). Isoindoline and 1,2,3,4-tetrahydroisoquinoline also formed the corresponding products (Table 2, Entries 16 and 17). Furthermore, when the reaction of **1g** with ethyl glyoxalate and **2a** was conducted on a gram-scale, the desired product **3ag** was produced in a similar yield to that afforded by the smaller scale reaction (Table 2, Entry 8).

We reasoned that functionalized furans are important core frameworks that are widely present in numerous bioactive natural products and pharmaceuticals,[4] and functionalized furans may also serve as versatile building blocks in organic synthesis because of their specific properties and latent functionality. Therefore, the development of a convenient and efficient method to prepare these frameworks is greatly desirable. We envisioned that the treatment of compound **3ag**, which was synthesized by the above-mentioned three-component reaction, with $CH_3I$ should provide ammonium cationic intermediate **A**. Upon considering the strong leaving ability of the quaternary ammonium salt and the aromatization of the oxygen-containing heterocycle, we

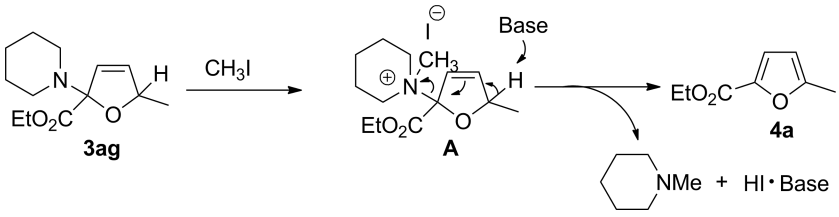
Table 2. The scope of the three-component reaction to afford 2,5-dihydrofurans.[a]




| Entry | ($R^1$, $R^2$) (**1**) | **2** | Yield [%] (**3**)[b] |
|---|---|---|---|
| 1 | Me, Me (**1a**) |  **2a** | 64 (**3aa**) |
| 2 | Et, Et (**1b**) | **2a** | 58 (**3ab**) |
| 3 | Me, Et (**1c**) | **2a** | 59 (**3ac**) |
| 4 | –$(CH_2)_3$– (**1d**) | **2a** | 57 (**3ad**) |
| 5 | –$(CH_2)_4$– (**1e**) | **2a** | 63 (**3ae**) |
| 6 | –$(CH_2)_5$– (**1f**) | **2a** | 62 (**3af**) |
| 7 | Me, H (**1g**) | **2a** | 56 (**3ag**) |
| 8[c] | Me, H (**1g**) | **2a** | 55 (**3ag**) |
| 9 | *n*-$C_5H_{11}$, H (**1h**) | **2a** | 65 (**3ah**) |
| 10 | Bn, H (**1i**) | **2a** | 57 (**3ai**) |
| 11 | Me, Me (**1a**) |  **2b** | 62 (**3ba**) |
| 12 | Me, Me (**1a**) |  **2c** | 61 (**3ca**) |
| 13 | Me, Me (**1a**) |  **2d** | 64 (**3da**) |
| 14 | Me, Me (**1a**) |  **2e** | 68 (**3ea**) |
| 15 | Me, Me (**1a**) |  **2f** | 65 (**3fa**) |
| 16 | Me, Me (**1a**) |  **2g** | 61 (**3ga**) |
| 17 | Me, Me (**1a**) |  **2h** | 67 (**3ha**) |

[a] Reagents and conditions: **1** (1.0 mmol), ethyl glyoxalate (1.2 mmol), **2** (1.2 mmol), MS (4 Å, 300 mg), and CuBr (0.2 mmol) in dioxane (3 mL) at 40 °C. [b] Isolated yield. [c] The reaction was carried on a 15 mmol scale of **1g** in THF (40 mL) with MS (4 Å, 1.5 g) and CuBr (10 mol-%).

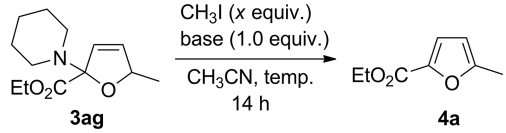



(1)

then expect intermediate **A** to form furan derivative **4a** in the presence of a base, see Equation (1).

To test our hypothesis, 2,5-dihydrofuran derivative **3ag** was treated with $CH_3I$ (5.0 equiv.) and $K_2CO_3$ (1.0 equiv.) in $CH_3CN$. After 14 h at 60 °C, the reaction yielded furan derivative **4a** in 77% yield along with the recovery of **3ag** in 14% yield (Table 3, Entry 1). When the loading of $CH_3I$ was increased to 10.0 equiv., a higher yield of **4a** was observed (Table 3, Entry 3). Further investigations of the base and reaction temperature suggest that the conditions reported in Entry 7 of Table 3 were most effective.

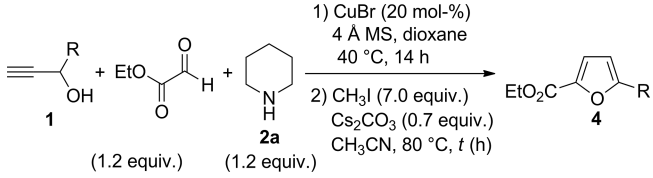
Table 3. Optimization of reaction conditions for preparing **4a**.[a]




| Entry | Base | X [equiv.] | *T* [°C] | % Yield **4a**[b] | % Recovery **3ag**[b] |
|---|---|---|---|---|---|
| 1 | $K_2CO_3$ | 5 | 60 | 77 | 14 |
| 2 | $K_2CO_3$ | 7 | 60 | 88 | 5 |
| 3 | $K_2CO_3$ | 10 | 60 | 91 | 1 |
| 4 | $Cs_2CO_3$ | 10 | 60 | 94 | 2 |
| 5 | $Li_2CO_3$ | 10 | 60 | 74 | 0 |
| 6 | $K_2CO_3$ | 10 | 80 | 93 | 0 |
| 7 | $Cs_2CO_3$ | 10 | 80 | 96 | 0 |

[a] The reactions were carried with **3ag** (1.0 mmol) in $CH_3CN$ (2 mL). [b] NMR yield.

Table 4. The scope of the three-component formation of 2,5-disubstituted furans.[a]




| Entry | R | *t* [h] | % Yield **4**[b] |
|---|---|---|---|
| 1 | H (**1j**) | 19 | 50 (**4b**) |
| 2 | Me (**1 g**) | 17.5 | 56 (**4a**) |
| 3 | $n$-$C_5H_{11}$ (**1h**) | 19 | 65 (**4c**) |
| 4[c] | $n$-$C_5H_{11}$ (**1h**) | 19 | 56 (**4c**) |
| 5 | Bn (**1i**) | 19 | 64 (**4d**) |
| 6[c] | Bn (**1i**) | 19 | 60 (**4d**) |
| 7 | Ph (**1k**) | 18.5 | 57 (**4e**) |
| 8[c] | Ph (**1k**) | 18.5 | 61 (**4e**) |
| 9 | 2-naphthyl (**1l**) | 19 | 58 (**4f**) |
| 10 | 2-furyl (**1m**) | 18.5 | 58 (**4g**) |
| 11 | (*E*)-styryl (**1n**) | 18.5 | 62 (**4h**) |
| 12 | (*E*)-hex-1-en-1-yl (**1o**) | 18.5 | 64 (**4i**) |
| 13[c] | (*E*)-hex-1-en-1-yl (**1o**) | 18.5 | 58 (**4i**) |

[a] Reagents and conditions: (step 1) **1** (1.0 mmol), ethyl glyoxalate (1.2 mmol), **2** (1.2 mmol), and MS (4 Å, 300 mg) in dioxane (3 mL); (step 2) $CH_3I$ (7.0 mmol), $Cs_2CO_3$ (0.7 mmol), and $CH_3CN$ (5 mL). [b] Isolated yield. [c] $K_2CO_3$ was used as the base.

Subsequently, an efficient two-step sequence to prepare furan derivatives **4a** from propargylic alcohols **1g**, ethyl glyoxalate, and piperidine **2a** was developed. After a simple filtration to remove the copper catalyst, the crude 2,5-dihydrofuran derivative **3ag** was then treated with 0.7 equiv. of $Cs_2CO_3$ and 7.0 equiv. of $CH_3I$ in $CH_3CN$ at 80 °C for 17.5 h to afford the corresponding product **4a** in 56% overall yield (Table 4, Entry 2). To demonstrate the generality of this protocol, we extended the scope to various propargylic alcohols. As shown in Table 4, all products were obtained in good yields. In some cases, $K_2CO_3$ was found to be equally efficient in this transformation.

## Conclusions

In summary, we have developed a simple, efficient, and mild synthesis of 2,5-dihydrofurans by employing a copper-catalyzed cascade three-component reaction with readily available propargylic alcohols, ethyl glyoxalate, and amines. The 2,5-disubstituted furans can also be prepared by a similar domino three-component reaction followed by a $CH_3I$-promoted aromatization. Further investigations including practical applications of this method are currently underway in our laboratory.

## Experimental Section

**General Methods:** All reactions were carried out in oven-dried Schlenk tubes. CuBr (98%) was purchased from Acros and kept in a glove box, and ethyl glyoxalate (50% in toluene) was purchased from Alfa Aesar. Molecular sieves (4 Å) were purchased from Alfa Aesar and kept in glove box after activation. (To activate, the molecular sieves were heated at 450 °C for 10 h in a Muffle furnace, removed after cooling to 200 °C, and then kept in a glove box to cool to room temperature). Dioxane was dried by using sodium wire with benzophenone as the indicator and then distilled freshly before use. $CH_3CN$ was dried with calcium hydride before distillation. Other reagents were used as received without further treatment. The reported temperatures refer to the temperature of the oil bath.

**Typical Procedure for the Synthesis of 2-(Ethoxycarbonyl)-5,5-dimethyl-2-(piperidin-1-yl)-2,5-dihydrofuran (3aa):** To a flame-dried Schlenk tube were added CuBr (98% purity, 29.2 mg, 0.2 mmol) and MS (4 Å, 300.0 mg) under Ar. Then, **1a** (84.1 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg,

1.2 mmol) in dioxane (1.0 mL), and **2a** (102.5 mg, 1.2 mmol) in dioxane (1.0 mL) were added sequentially under Ar. The resulting mixture was then stirred at 40 °C until the reaction reached completion, as monitored by TLC (14 h). The crude reaction mixture was filtered through a short pad of silica gel [diethyl ether (30 mL)]. After evaporation of the filtrate, the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 20:1) to afford **3aa** (161.5 mg, 64%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.96 (d, $J$ = 5.7 Hz, 1 H, =CH), 5.64 (d, $J$ = 5.7 Hz, 1 H, =CH), 4.37–4.16 (m, 2 H, $OCH_2$), 2.72–2.61 (m, 2 H, $NCH_2$), 2.50–2.40 (m, 2 H, $NCH_2$), 1.70–1.54 (m, 4 H, 2 $CH_2$), 1.50–1.35 (m, 8 H, $CH_2$ and 2 $CH_3$), 1.29 (t, $J$ = 7.1 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.2, 139.6, 125.6, 106.4, 87.7, 61.2, 47.4, 27.5, 26.9, 25.8, 24.2, 14.0 ppm. MS (ESI): $m/z$ = 254 [M + H]$^+$, 276 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 2975, 2934, 2854, 2820, 1747, 1467, 1454, 1444, 1361, 1336, 1311, 1248, 1216, 1172, 1120, 1093, 1081, 1032 cm$^{-1}$. HRMS (ESI): calcd. for $C_{14}H_{24}NO_3$ [M + H]$^+$ 254.1751; found 254.1754.

**2-(Ethoxycarbonyl)-5,5-diethyl-2-(piperidin-1-yl)-2,5-dihydrofuran (3ab):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.2 mg), **1b** (98% purity, 115.3 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.7 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.0 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 20:1) to afford **3ab** (163.7 mg, 58%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.01 (d, $J$ = 6.0 Hz, 1 H, =CH), 5.73 (d, $J$ = 6.0 Hz, 1 H, =CH), 4.33–4.16 (m, 2 H, $OCH_2$), 2.73–2.61 (m, 2 H, $NCH_2$), 2.52–2.40 (m, 2 H, $NCH_2$), 1.80–1.50 (m, 8 H, 4 $CH_2$), 1.50–1.38 (m, 2 H, $CH_2$), 1.28 (t, $J$ = 7.1 Hz, 3 H, $CH_3$), 0.96 (t, $J$ = 7.5 Hz, 3 H, $CH_3$), 0.85 (t, $J$ = 7.7 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.1, 137.7, 126.3, 105.7, 93.5, 61.1, 47.6, 29.9, 29.5, 26.0, 24.4, 14.1, 8.7, 8.4 ppm. MS (ESI): $m/z$ = 304 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 2964, 2935, 2879, 2853, 2819, 1748, 1456, 1445, 1383, 1311, 1274, 1256, 1226, 1206, 1164, 1119, 1085, 1061, 1034 cm$^{-1}$. HRMS (ESI): calcd. for $C_{16}H_{28}NO_3$ [M + H]$^+$ 282.2064; found 282.2070.

**2-(Ethoxycarbonyl)-5-ethyl-5-methyl-2-(piperidin-1-yl)-2,5-dihydrofuran (3ac):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1c** (98% purity, 101.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.7 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.3 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 10:1) to afford **3ac** (159.3 mg, 59%; mixture of two diastereomers, 1.26:1 *dr*) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.03–5.93 (m, 1 H, =CH), 5.73–5.64 (m, 1 H, =CH), 4.39–4.15 (m, 2 H, $OCH_2$), 2.73–2.59 (m, 2 H, $NCH_2$), 2.52–2.38 (m, 2 H, $NCH_2$), 1.76–1.51 (m, 6 H, 3 $CH_2$), 1.50–1.38 (m, 2 H, $CH_2$), 1.37–1.23 (m, 6 H, 2 $CH_3$), [0.99 (t, $J$ = 7.5 Hz, 1.33 H, minor isomer), 0.90 (t, $J$ = 7.4 Hz, 1.67 H, major isomer), 3 H, $CH_3$] ppm. MS (ESI): $m/z$ = 268 [M + H]$^+$, 290 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 2934, 2853, 2819, 1748, 1627, 1454, 1369, 1256, 1231, 1211, 1168, 1119, 1093, 1083, 1033, 1011 cm$^{-1}$. HRMS (ESI): calcd. for $C_{15}H_{26}NO_3$ [M + H]$^+$ 268.1907; found 268.1911.

**6-(Ethoxycarbonyl)-6-(piperidin-1-yl)-5-oxaspiro[3.4]oct-7-ene (3ad):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.1 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1d** (95.7 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.4 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.1 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, from 15:1 to 10:1) to afford **3ad** (151.3 mg, 57%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.25 (d, $J$ = 5.4 Hz, 1 H, =CH), 5.66 (d, $J$ = 5.7 Hz, 1 H, =CH), 4.33–4.14 (m, 2 H, $OCH_2$), 2.70–2.32 (m, 6 H, 2 $NCH_2$ and $CH_2$), 2.25–2.08 (m, 2 H, $CH_2$), 1.81–1.38 (m, 8 H, 4 $CH_2$), 1.27 (t, $J$ = 6.9 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 170.6, 136.6, 125.7, 106.6, 89.8, 61.3, 47.1, 35.3, 35.2, 25.6, 24.2, 14.0, 11.4 ppm. MS (ESI): $m/z$ = 266 [M + H]$^+$. IR (neat): $\tilde{\nu}$ = 2981, 2934, 2852, 2820, 1748, 1620, 1468, 1453, 1344, 1312, 1249, 1221, 1186, 1153, 1118, 1092, 1075, 1031 cm$^{-1}$. HRMS (ESI): calcd. for $C_{15}H_{24}NO_3$ [M + H]$^+$ 266.1751; found 266.1753.

**2-(Ethoxycarbonyl)-2-(piperidin-1-yl)-1-oxaspiro[4.4]non-3-ene (3ae):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.5 mg, 0.2 mmol), MS (4 Å, 300.0 mg), **1e** (98% purity, 112.9 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.7 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.5 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 20:1) to afford **3ae** (176.6 mg, 63%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.94 (d, $J$ = 5.7 Hz, 1 H, =CH), 5.64 (d, $J$ = 5.7 Hz, 1 H, =CH), 4.37–4.11 (m, 2 H, $OCH_2$), 2.68–2.57 (m, 2 H, $NCH_2$), 2.47–2.36 (m, 2 H, $NCH_2$), 2.14–2.00 (m, 1 H), 1.96–1.80 (m, 3 H), 1.78–1.51 (m, 8 H, 4 $CH_2$), 1.49–1.37 (m, 2 H, $CH_2$), 1.28 (t, $J$ = 7.1 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.2, 138.1, 125.6, 106.2, 97.8, 61.2, 47.4, 38.5, 38.1, 25.7, 24.7, 24.6, 24.3, 14.0 ppm. MS (ESI): $m/z$ = 302 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 2934, 2852, 2819, 1747, 1625, 1469, 1444, 1345, 1256, 1233, 1214, 1173, 1121, 1101, 1077, 1034, 1006 cm$^{-1}$. HRMS (ESI): calcd. for $C_{16}H_{26}NO_3$ [M + H]$^+$ 280.1907; found 280.1912.

**2-(Ethoxycarbonyl)-2-(piperidin-1-yl)-1-oxaspiro[4.5]dec-3-ene (3af):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.3 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1f** (97% purity, 127.3 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 244.9 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.1 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 20:1) to afford **3af** (182.5 mg, 62%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.13 (d, $J$ = 6.0 Hz, 1 H, =CH), 5.68 (d, $J$ = 6.0 Hz, 1 H, =CH), 4.34–4.13 (m, 2 H, $OCH_2$), 2.70–2.59 (m, 2 H, $NCH_2$), 2.49–2.39 (m, 2 H, $NCH_2$), 1.87–1.35 (m, 16 H, 8 $CH_2$), 1.28 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.5, 138.0, 126.1, 105.7, 89.7, 61.2, 47.5, 37.2, 36.4, 25.8, 25.3, 24.3, 23.3, 23.2, 14.0 ppm. MS (ESI): $m/z$ = 294 [M + H]$^+$. IR (neat): $\tilde{\nu}$ = 2964, 2935, 2879, 2853, 2819, 1748, 1627, 1455, 1445, 1383, 1311, 1256, 1226, 1206, 1164, 1119, 1094, 1085, 1062, 1035 cm$^{-1}$. HRMS (ESI): calcd. for $C_{17}H_{28}NO_3$ [M + H]$^+$ 294.2064; found 294.2069.

**2-(Ethoxycarbonyl)-5-methyl-2-(piperidin-1-yl)-2,5-dihydrofuran (3ag):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1g** (69.2 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.3 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography [petroleum ether (400 mL)/ethyl acetate (40 mL)/$Et_3N$ (0.3 mL)] to afford **3ag** (133.0 mg, 56%; mixture of two diastereomers, 1.5:1 *dr*) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = [6.06 (dd, $J_1$ = 6.0 Hz, $J_2$ = 1.5 Hz, 0.40 H, minor isomer), 5.98 (dd, $J_1$ = 5.9 Hz, $J_2$ = 1.4 Hz, 0.60 H, major isomer), 1 H, =CH], 5.75–5.69 (m, 1 H, =CH), 5.07–4.95 (m, 1 H, CH), 4.36–4.15 (m, 2 H, $OCH_2$), 2.76–2.60 (m, 2 H, $NCH_2$), 2.51–2.39 (m, 2 H, $NCH_2$), 1.70–1.51 (m, 4 H, 2 $CH_2$),

1.49–1.39 (m, 2 H, $CH_2$), 1.38–1.23 (m, 6 H, 2 $CH_3$) ppm. MS (ESI): *m*/*z* = 240 [M + H]$^+$, 262 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 3060, 2982, 2970, 2933, 2882, 2850, 2822, 2759, 1730, 1466, 1444, 1386, 1363, 1346, 1325, 1309, 1273, 1255, 1230, 1184, 1158, 1136, 1116, 1079, 1060, 1030 cm$^{-1}$. $C_{13}H_{21}NO_3$ (239.31): calcd. C 65.25, H 8.84, N 5.85; found C 65.35, H 8.91, N 5.86.

**Gram-Scale Preparation of 2-(Ethoxycarbonyl)-5-methyl-2-(piperidin-1-yl)-2,5-dihydrofuran (3ag):** To a flame-dried Schlenk tube were added CuBr (98% purity, 218.9 mg, 1.5 mmol) and MS (4 Å, 1.5001 g) under Ar. Then, **1g** (1.0538 g, 15 mmol) in THF (15 mL), ethyl glyoxalate (50% in toluene, 3.6758 g, 18 mmol) in THF (15 mL), and **2a** (1.5300 g, 18 mmol) in THF (10 mL) were added sequentially under Ar. The resulting mixture was stirred at 40 °C until the reaction reached completion, as monitored by TLC (14 h). The crude reaction mixture was filtered through a short pad of silica gel [diethyl ether (50 mL)]. After evaporation of the filtrate, the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 10:1) to afford **3ag** (1.9634 g, 55%; mixture of two diastereomers, 1.54:1 *dr*) as a liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = [6.05 (d, *J* = 6.0 Hz, 0.39 H, minor isomer), 5.98 (d, *J* = 6.0 Hz, 0.60 H, major isomer), 1 H, =CH], 5.76–5.68 (m, 1 H, =CH), 5.07–4.94 (m, 1 H, CH), 4.35–4.16 (m, 2 H, $OCH_2$), 2.76–2.60 (m, 2 H, $NCH_2$), 2.52–2.40 (m, 2 H, $NCH_2$), 1.69–1.51 (m, 4 H, 2 $CH_2$), 1.49–1.39 (m, 2 H, $CH_2$), 1.38–1.23 (m, 6 H, 2 $CH_3$) ppm.

**2-(Ethoxycarbonyl)-5-pentyl-2-(piperidin-1-yl)-2,5-dihydrofuran (3ah):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.0 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1h** (126.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.3 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.1 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 10:1) to afford **3ah** (193.3 mg, 65%; mixture of two diastereomers, 1.38:1 *dr*) as a liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = [6.08 (dd, $J_1$ = 6.0 Hz, $J_2$ = 1.6 Hz, 0.42 H, minor isomer), 6.03 (dd, $J_1$ = 5.8 Hz, $J_2$ = 1.4 Hz, 0.58 H, major isomer), 1 H, =CH], [5.75 (dd, $J_1$ = 6.0 Hz, $J_2$ = 2.4 Hz, 0.42 H, minor isomer), 5.72 (dd, $J_1$ = 5.8 Hz, $J_2$ = 2.6 Hz, 0.58 H, major isomer), 1 H, =CH], 4.87–4.82 (m, 1 H, CH), 4.32–4.16 (m, 2 H, $OCH_2$), 2.74–2.61 (m, 2 H, $NCH_2$), 2.51–2.42 (m, 2 H, $NCH_2$), 1.75–1.48 (m, 6 H, 3 $CH_2$), 1.47–1.24 (m, 11 H, 4 $CH_2$ and $CH_3$), 0.94–0.84 (m, 3 H, $CH_3$) ppm. MS (ESI): *m*/*z* = 296 [M + H]$^+$. IR (neat): $\tilde{\nu}$ = 2931, 2855, 1747, 1467, 1454, 1444, 1384, 1365, 1330, 1310, 1255, 1222, 1182, 1137, 1092, 1067, 1031 cm$^{-1}$. $C_{17}H_{29}NO_3$ (295.42): calcd. C 69.12, H 9.89, N 4.74; found C 68.96, H 10.06, N 4.96.

**5-Benzyl-2-(ethoxycarbonyl)-2-(piperidin-1-yl)-2,5-dihydrofuran (3ai):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.3 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1i** (146.4 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (103.0 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 10:1) to afford **3ai** (179.4 mg, 57%; mixture of two diastereomers, 1.08:1 *dr*) as a liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.32–7.18 (m, 5 H, Ar-H), [6.01 (dd, $J_1$ = 6.0 Hz, $J_2$ = 1.2 Hz, 0.47 H, minor isomer), 5.97 (dd, $J_1$ = 5.8 Hz, $J_2$ = 1.8 Hz, 0.52 H, major isomer), 1 H, =CH], [5.78 (dd, $J_1$ = 5.8 Hz, $J_2$ = 2.2 Hz, minor isomer, 0.48 H), 5.75 (dd, $J_1$ = 5.8 Hz, $J_2$ = 2.6 Hz, 0.52 H, major isomer), 1 H, =CH], 5.09–4.98 (m, 1 H, CH), 4.36–4.15 (m, 2 H, $OCH_2$), 3.25–3.13 (m, 1 H, one proton from $ArCH_2$), 2.79–2.63 (m, 3 H, one proton of $ArCH_2$ and $NCH_2$), 2.51–2.40 (m, 2 H, $NCH_2$), 1.68–1.51 (m, 4 H, 2 $CH_2$), 1.49–1.38 (m, 2 H, $CH_2$), [1.32 (t, *J* = 7.0 Hz, 1.49 H, minor isomer), 1.26 (t, *J* = 7.2 Hz, 1.75 H, major isomer), 3 H, $CH_3$] ppm. MS (ESI): *m*/*z* = 316 [M + H]$^+$. IR (neat): $\tilde{\nu}$ = 3055, 2928, 1737, 1494, 1467, 1452, 1349, 1331, 1313, 1273, 1255, 1226, 1190, 1136, 1111, 1092, 1078, 1063, 1051, 1026 cm$^{-1}$. HRMS (ESI): calcd. for $C_{19}H_{26}NO_3$ [M + H]$^+$ 316.1907; found 316.1907.

**2-[5,6-Dihydropyridin-1(2*H*)-yl]-2-(ethoxycarbonyl)-5,5-dimethyl-2,5-dihydrofuran (3ba):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.0 mg), **1a** (83.9 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.9 mg, 1.2 mmol) in dioxane (1.0 mL), and **2b** (100.0 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, from 10:1 to 5:1) to afford **3ba** (156.0 mg, 62%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.99 (d, *J* = 5.4 Hz, 1 H, =CH), 5.79–5.62 (m, 3 H, 3 =CH), 4.37–4.17 (m, 2 H, $OCH_2$), 3.23 (br. d, *J* = 16.2 Hz, 1 H, one proton from $NCH_2C$=), 3.08 (br. d, *J* = 16.2 Hz, 1 H, one proton from $NCH_2C$=), 2.82–2.72 (m, 1 H, one proton from $NCH_2$), 2.70–2.59 (m, 1 H, one proton from $NCH_2$), 2.30–2.01 (m, 2 H, $CH_2$), 1.43 (s, 3 H, $CH_3$), 1.40 (s, 3 H, $CH_3$), 1.30 (t, *J* = 7.1 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.0, 140.0, 125.3, 125.1, 124.9, 105.8, 88.0, 61.4, 45.5, 43.8, 27.6, 27.0, 26.4, 14.1 ppm. MS (ESI): *m*/*z* = 274 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 3033, 2974, 2833, 1747, 1660, 1627, 1464, 1447, 1380, 1361, 1336, 1299, 1250, 1230, 1211, 1160, 1132, 1090, 1044, 1031 cm$^{-1}$. HRMS (ESI): calcd. for $C_{14}H_{22}NO_3$ [M + H]$^+$ 252.1594; found 252.1602.

**2-(Ethoxycarbonyl)-5,5-dimethyl-2-(pyrrolidin-1-yl)-2,5-dihydrofuran (3ca):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.0 mg, 0.2 mmol), MS (4 Å, 300.0 mg), **1a** (84.1 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 244.2 mg, 1.2 mmol) in dioxane (1.0 mL), and **2c** (85.7 mg, 1.2 mmol in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography [petroleum ether (400 mL)/ethyl acetate (40 mL)/$Et_3N$ (0.3 mL)] to afford **3ca** (145.1 mg, 61%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.94 (d, *J* = 5.7 Hz, 1 H, =CH), 5.74 (d, *J* = 5.7 Hz, 1 H, =CH), 4.36–4.19 (m, 2 H, $OCH_2$), 2.84–2.62 (m, 4 H, 2 $NCH_2$), 1.86–1.72 (m, 4 H, 2 $CH_2$), 1.41 (s, 3 H, $CH_3$), 1.40 (s, 3 H, $CH_3$), 1.31 (t, *J* = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 170.8, 139.0, 126.2, 103.0, 87.4, 61.2, 46.0, 27.8, 26.9, 23.7, 14.0 ppm. MS (ESI): *m*/*z* = 240 [M + H]$^+$. IR (neat): $\tilde{\nu}$ = 2970, 2932, 2873, 1748, 1628, 1462, 1361, 1338, 1242, 1148, 1086, 1040, 1029, 1003 cm$^{-1}$. HRMS (ESI): calcd. for $C_{13}H_{22}NO_3$ [M + H]$^+$ 240.1594,; found 240.1596.

**2-(2,5-Dihydro-1*H*-pyrrol-1-yl)-2-(ethoxycarbonyl)-5,5-dimethyl-2,5-dihydrofuran (3da):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.0 mg), **1a** (84.7 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2d** (83.8 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 10:1) to afford **3da** (152.5 mg, 64%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.97 (d, *J* = 6.0 Hz, 1 H, =CH), 5.77 (d, *J* = 6.0 Hz, 1 H, =CH), 5.73 (s, 2 H, 2 CH=), 4.35–4.20 (m, 2 H, $OCH_2$), 3.77–3.58 (m, 4 H, 2 $NCH_2$), 1.41 (s, 6 H, 2 $CH_3$), 1.31 (t, *J* = 7.1 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 170.7, 139.6, 126.6, 126.3, 102.9, 87.6, 61.4, 53.1, 27.9, 27.1, 14.1 ppm. MS (ESI): *m*/*z* = 260 [M + Na]$^+$. IR (neat): $\tilde{\nu}$ = 3071, 2977, 2933, 2864, 2831, 1742, 1626, 1466, 1445, 1359, 1343, 1301, 1263, 1239, 1191, 1156, 1085, 1032, 1010 cm$^{-1}$.

HRMS (ESI): calcd. for $C_{13}H_{20}NO_3$ $[M + H]^+$ 238.1438; found 238.1439.

**2-(Dibutylamino)-2-(ethoxycarbonyl)-5,5-dimethyl-2,5-dihydrofuran (3ea):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.4 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1a** (83.1 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2e** (155.0 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 40:1) to afford **3ea** (201.1 mg, 68%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.92 (d, $J$ = 5.7 Hz, 1 H, =CH), 5.67 (d, $J$ = 5.7 Hz, 1 H, =CH), 4.28–4.15 (m, 2 H, $OCH_2$), 2.70–2.44 (m, 4 H, 2 $NCH_2$), 1.50–1.34 (m, 10 H, 2 $CH_2$ and 2 $CH_3$), 1.33–1.18 (m, 7 H, 2 $CH_2$ and $CH_3$), 0.88 (t, $J$ = 7.4 Hz, 6 H, 2 $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.6, 139.2, 126.9, 107.1, 87.1, 61.1, 49.4, 31.7, 27.6, 27.0, 20.4, 14.0, 13.9 ppm. MS (ESI): $m/z$ = 298 $[M + H]^+$. IR (neat): $\tilde{\nu}$ = 2958, 2933, 2872, 1748, 1627, 1464, 1378, 1361, 1335, 1244, 1224, 1182, 1124, 1083, 1066, 1034 cm$^{-1}$. HRMS (ESI): calcd. for $C_{17}H_{32}NO_3$ $[M + H]^+$ 298.2377; found 298.2383.

**2-(Diallylamino)-2-(ethoxycarbonyl)-5,5-dimethyl-2,5-dihydrofuran (3fa):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1a** (84.5 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg, 1.2 mmol) in dioxane (1.0 mL), and **2f** (117.0 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 40:1) to afford **3fa** (171.8 mg, 65%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.95 (d, $J$ = 5.7 Hz, 1 H, =CH), 5.93–5.78 (m, 2 H, 2 =CH), 5.69 (d, $J$ = 5.7 Hz, 1 H, =CH), 5.13 (d, $J$ = 17.1 Hz, 2 H, 2 =CH), 5.04 (d, $J$ = 9.9 Hz, 2 H, 2 =CH), 4.28–4.12 (m, 2 H, $OCH_2$), 3.32 (dd, $J_1$ = 15.2 Hz, $J_2$ = 5.9 Hz, 2 H, 2× one proton of $NCH_2$), 3.21 (dd, $J_1$ = 15.3 Hz, $J_2$ = 6.6 Hz, 2 H, 2× one proton of $NCH_2$), 1.393 (s, 3 H, $CH_3$), 1.385 (s, 3 H, $CH_3$), 1.28 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 171.1, 139.7, 136.9, 126.5, 116.2, 106.2, 87.5, 61.2, 51.3, 27.6, 27.1, 14.0 ppm. MS (ESI): $m/z$ = 288 $[M + Na]^+$. IR (neat): $\tilde{\nu}$ = 3077, 2976, 2931, 2846, 1749, 1642, 1463, 1447, 1418, 1361, 1337, 1259, 1234, 1172, 1086, 1033 cm$^{-1}$. HRMS (ESI): calcd. for $C_{15}H_{24}NO_3$ $[M + H]^+$ 266.1751; found 266.1755.

**2-(Ethoxycarbonyl)-2-(isoindolin-2-yl)-5,5-dimethyl-2,5-dihydrofuran (3ga):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.8 mg, 0.2 mmol), MS (4 Å, 300.2 mg), **1a** (85.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.7 mg, 1.2 mmol) in dioxane (1.0 mL), and **2g** (143.1 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, 10:1) to afford **3ga** (176.0 mg, 61%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.18 (s, 4 H, Ar-H), 6.03 (d, $J$ = 5.7 Hz, 1 H, =CH), 5.85 (d, $J$ = 5.7 Hz, 1 H, =CH), 4.30 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 4.25–4.17 (m, 2 H, $ArCH_2$), 4.13–4.04 (m, 2 H, $ArCH_2$), 1.43 (s, 3 H, $CH_3$), 1.42 (s, 3 H, $CH_3$), 1.33 (t, $J$ = 6.9 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 170.6, 139.9, 139.0, 126.7, 126.2, 122.4, 102.9, 87.9, 61.6, 52.2, 28.0, 27.3, 14.2 ppm. MS (ESI): $m/z$ = 310 $[M + Na]^+$. IR (neat): $\tilde{\nu}$ = 2972, 2834, 1747, 1463, 1442, 1378, 1362, 1338, 1327, 1296, 1277, 1239, 1197, 1181, 1171, 1141, 1085, 1064, 1032 cm$^{-1}$. HRMS (ESI): calcd. for $C_{17}H_{22}NO_3$ $[M + H]^+$ 288.1594; found 288.1601.

**2-[3,4-Dihydroisoquinolin-2(1*H*)-yl]-2-(ethoxycarbonyl)-5,5-dimethyl-2,5-dihydrofuran (3ha):** By following the same procedure as that described for **3aa**, the reaction of CuBr (98% purity, 29.4 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1a** (83.6 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2h** (159.5 mg, 1.2 mmol) in dioxane (1.0 mL) gave the crude product, which was purified by column chromatography (petroleum ether/ethyl acetate, from 20:1 to 10:1) to afford **3ha** (201.7 mg, 67%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.14–7.04 (m, 3 H, Ar-H), 7.03–6.95 (m, 1 H, Ar-H), 6.05 (d, $J$ = 6.0 Hz, 1 H, =CH), 5.75 (d, $J$ = 5.4 Hz, 1 H, =CH), 4.38–4.19 (m, 2 H, $OCH_2$), 3.92 (d, $J$ = 14.7 Hz, 1 H, one proton of $ArCH_2$), 3.74 (d, $J$ = 14.7 Hz, 1 H, one proton of $ArCH_2$), 3.02–2.79 (m, 4 H, 2 $CH_2$), 1.45 (s, 3 H, $CH_3$), 1.41 (s, 3 H, $CH_3$), 1.30 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 170.9, 140.3, 134.6, 134.2, 128.5, 126.6, 125.8, 125.4, 125.3, 105.7, 88.2, 61.5, 48.7, 44.7, 29.5, 27.6, 27.1, 14.1 ppm. MS (ESI): $m/z$ = 324 $[M + Na]^+$. IR (neat): $\tilde{\nu}$ = 2975, 2928, 2831, 1746, 1498, 1464, 1384, 1361, 1335, 1275, 1247, 1229, 1148, 1087, 1075, 1034, 1003 cm$^{-1}$. HRMS (ESI): calcd. for $C_{18}H_{24}NO_3$ $[M + H^+]$ 302.1751; found 302.1749.

**Typical Procedure for the Synthesis of 2-(Ethoxycarbonyl)-5-methylfuran (4a):** To a flame-dried Schlenk tube were added CuBr (98% purity, 29.3 mg, 0.2 mmol) and MS (4 Å, 300.2 mg) under Ar. Then, **1g** (70.2 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.3 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.4 mg, 1.2 mmol) in dioxane (1.0 mL) were added sequentially under Ar. The resulting mixture was stirred at 40 °C until the reaction reached completion, as monitored by TLC (14 h). The crude reaction mixture was filtered through a short pad of silica gel [diethyl ether (30 mL)]. After evaporation of the filtrate, the crude product was used in the next step without further treatment. To another flame-dried Schlenk tube were added $Cs_2CO_3$ (228.7 mg, 0.7 mmol), the crude product in $CH_3CN$ (4.0 mL), and $CH_3I$ ($d$ = 2.28 g mL$^{-1}$, 0.44 mL, 7.0 mmol) sequentially under Ar. The mixture was stirred at 80 °C until the reaction reached completion, as monitored by TLC (17.5 h). The crude reaction mixture was filtered through a short pad of silica gel [diethyl ether (30 mL)]. After evaporation of the filtrate, the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate, 40:1) to afford **4a** (85.7 mg, 56%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.08 (d, $J$ = 3.3 Hz, 1 H, CH=), 6.12 (d, $J$ = 3.3 Hz, 1 H, CH=), 4.35 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.38 (s, 3 H, $CH_3$), 1.37 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.7, 156.9, 143.1, 119.1, 108.2, 60.5, 14.2, 13.8 ppm. MS (EI): $m/z$ (%) = 154 (27.95) $[M]^+$, 109 (100). IR (neat): $\tilde{\nu}$ = 1716, 1599, 1533, 1447, 1371, 1299, 1259, 1209, 1135, 1019 cm$^{-1}$. HRMS (EI): calcd. for $C_8H_{10}O_3$ $[M]^+$ 154.0630; found 154.0632.

**2-(Ethoxycarbonyl)furan (4b):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1j** (56.1 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.3 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.3 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g mL$^{-1}$, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (from petroleum ether to petroleum ether/ethyl acetate, 100:1) afforded **4b** (70.1 mg, 50%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.58 (d, $J$ = 0.6 Hz, 1 H, CH=), 7.18 (d, $J$ = 3.3 Hz, 1 H, CH=), 6.51 (dd, $J_1$ = 3.3 Hz, $J_2$ = 1.8 Hz, 1 H, CH=), 4.37 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 1.38 (t, $J$ = 7.1 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.6, 146.1, 144.8, 117.6, 111.7, 60.8, 14.2 ppm. MS (EI): $m/z$ (%) = 140 (17.88) $[M]^+$, 44 (100). IR (neat): $\tilde{\nu}$ = 1718, 1581, 1571, 1475, 1400, 1390, 1367, 1295, 1260, 1231, 1182, 1114, 1076, 1009 cm$^{-1}$. HRMS (EI): calcd. for $C_7H_8O_3$ $[M]^+$ 140.0473; found 140.0474.

**2-(Ethoxycarbonyl)-5-pentylfuran (4c):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.4 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1h** (127.1 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 246.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (103.1 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.3 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g mL$^{-1}$, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4c** (136.6 mg, 65%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.09 (d, $J$ = 3.3 Hz, 1 H, CH=), 6.11 (d, $J$ = 3.3 Hz, 1 H, CH=), 4.34 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.68 (t, $J$ = 7.8 Hz, 2 H, $CH_2$), 1.73–1.60 (m, 2 H, $CH_2$), 1.41–1.25 (m, 7 H, 2 $CH_2$ and $CH_3$), 0.90 (t, $J$ = 6.8 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.4, 158.8, 143.0, 118.9, 107.3, 60.5, 31.2, 28.2, 27.3, 22.2, 14.3, 13.8 ppm. MS (EI): $m/z$ (%) = 210 (32.33) [M]$^+$, 153 (100). IR (neat): $\tilde{\nu}$ = 1717, 1595, 1530, 1520, 1465, 1382, 1368, 1298, 1259, 1204, 1135, 1091, 1014 cm$^{-1}$. HRMS (EI): calcd. for $C_{12}H_{18}O_3$ [M]$^+$ 210.1256, found 210.1254.

**Preparation of 2-(Ethoxycarbonyl)-5-pentylfuran (4c) with $K_2CO_3$ as the Base:** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.3 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1h** (126.1 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.2 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.4 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $K_2CO_3$ (97.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g mL$^{-1}$, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4c** (116.8 mg, 56%) as a liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.08 (d, $J$ = 4.0 Hz, 1 H, CH=), 6.11 (d, $J$ = 3.6 Hz, 1 H, CH=), 4.34 (q, $J$ = 7.2 Hz, 2 H, $OCH_2$), 2.68 (t, $J$ = 7.6 Hz, 2 H, $CH_2$), 1.73–1.63 (m, 2 H, $CH_2$), 1.40–1.27 (m, 7 H, 2 $CH_2$ and $CH_3$), 0.90 (t, $J$ = 6.6 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 161.4, 158.8, 143.0, 118.9, 107.3, 60.5, 31.2, 28.2, 27.3, 22.2, 14.3, 13.8 ppm.

**5-Benzyl-2-(ethoxycarbonyl)furan (4d):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.0 mg, 0.2 mmol), MS (4 Å, 300.2 mg), **1i** (146.9 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 246.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.9 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.7 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, from 200:1 to 100:1) afforded **4d** (148.4 mg, 64%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.36–7.19 (m, 5 H, Ar-H), 7.08 (d, $J$ = 3.3 Hz, 1 H, CH=), 6.04 (d, $J$ = 3.3 Hz, 1 H, CH=), 4.33 (q, $J$ = 7.2 Hz, 2 H, $OCH_2$), 4.02 (s, 2 H, $CH_2$), 1.35 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 159.4, 158.8, 143.6, 136.6, 128.8, 128.6, 126.8, 118.9, 108.7, 60.6, 34.6, 14.3 ppm. MS (EI): $m/z$ (%) = 230 (55.68) [M]$^+$, 157 (100). IR (neat): $\tilde{\nu}$ = 1713, 1595, 1518, 1496, 1454, 1383, 1367, 1297, 1205, 1127, 1015 cm$^{-1}$. HRMS (EI): calcd. for $C_{14}H_{14}O_3$ [M]$^+$ 230.0943; found 230.0941.

**Preparation of 5-Benzyl-2-(ethoxycarbonyl)furan (4d) with $K_2CO_3$ as the Base:** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.5 mg, 0.2 mmol), MS (4 Å, 300.2 mg), **1i** (146.2 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.2 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.4 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $K_2CO_3$ (97.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, from 200:1 to 100:1) afforded **4d** (138.2 mg, 60%) as a liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.34–7.27 (m, 2 H, Ar-H), 7.26–7.20 (m, 3 H, Ar-H), 7.07 (d, $J$ = 3.2 Hz, 1 H, CH=), 6.05 (d, $J$ = 3.2 Hz, 1 H, CH=), 4.33 (q, $J$ = 7.2 Hz, 2 H, $OCH_2$), 4.02 (s, 2 H, $CH_2$), 1.35 (t, $J$ = 7.0 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 159.5, 158.8, 143.6, 136.7, 128.8, 128.6, 126.8, 118.9, 108.7, 60.7, 34.7, 14.3 ppm.

**2-(Ethoxycarbonyl)-5-phenylfuran (4e):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.0 mg, 0.2 mmol), MS (4 Å, 300.2 mg), **1k** (134.7 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.7 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.7 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4e** (124.2 mg, 57%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.80–7.73 (m, 2 H, Ar-H), 7.43–7.28 (m, 3 H, Ar-H), 7.22 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.71 (d, $J$ = 3.6 Hz, 1 H, CH=), 4.37 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 1.38 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.7, 157.3, 143.8, 129.4, 128.8, 128.7, 124.7, 119.7, 106.7, 60.7, 14.3 ppm. MS (EI): $m/z$ (%) = 216 (100) [M$^+$]. IR (neat): $\tilde{\nu}$ = 1710, 1573, 1529, 1479, 1449, 1373, 1298, 1270, 1216, 1135, 1017 cm$^{-1}$. HRMS (EI): calcd. for $C_{13}H_{12}O_3$ [M]$^+$ 216.0786; found 216.0784.

**Preparation of 2-(Ethoxycarbonyl)-5-phenylfuran (4e) with $K_2CO_3$ as the Base:** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1k** (134.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.3 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $K_2CO_3$ (97.2 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4e** (132.0 mg, 61%) as a liquid. $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.79–7.74 (m, 2 H, Ar-H), 7.43–7.37 (m, 2 H, Ar-H), 7.35–7.29 (m, 1 H, Ar-H), 7.22 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.71 (d, $J$ = 3.2 Hz, 1 H, CH=), 4.37 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 1.38 (t, $J$ = 6.8 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 158.8, 157.4, 143.8, 129.5, 128.8, 128.7, 124.7, 119.7, 106.7, 60.8, 14.3 ppm.

**2-(Ethoxycarbonyl)-5-(naphthalen-2-yl)furan (4f):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.5 mg, 0.2 mmol), MS (4 Å, 300.0 mg), **1l** (183.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.9 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (103.0 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 100:1) afforded **4f** (154.3 mg, 58%) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.26 (s, 1 H, Ar-H), 7.89–7.74 (m, 4 H, Ar-H), 7.51–7.40 (m, 2 H, Ar-H), 7.24 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.79 (d, $J$ = 3.6 Hz, 1 H, CH=), 4.39 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 1.40 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.8, 157.4, 143.9, 133.24, 133.18, 128.5, 128.3, 127.7, 126.7, 126.61, 126.57, 123.8, 123.3, 119.8, 107.2, 60.8, 14.3 ppm. MS (EI): $m/z$ (%) = 266 (100) [M]$^+$. IR (neat): $\tilde{\nu}$ = 1719,

1582, 1526, 1496, 1476, 1459, 1439, 1379, 1365, 1338, 1301, 1277, 1268, 1232, 1215, 1160, 1145, 1060, 1023 $cm^{-1}$. HRMS (EI): calcd. for $C_{17}H_{14}O_3$ $[M]^+$ 266.0943; found 266.0945.

**5-(Ethoxycarbonyl)-2,2′-bifuran (4g):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.2 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1m** (122.6 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 246.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.5 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4g** (119.7 mg, 58%) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.46 (d, $J$ = 1.5 Hz, 1 H, CH=), 7.21 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.81 (d, $J$ = 3.3 Hz, 1 H, CH=), 6.62 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.49 (dd, $J_1$ = 3.3 Hz, $J_2$ = 1.5 Hz, 1 H, CH=), 4.37 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 1.38 (t, $J$ = 7.1 Hz, 3 H, $CH_3$) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 158.6, 149.6, 145.2, 143.4, 143.0, 119.5, 111.7, 108.0, 106.5, 60.8, 14.2 ppm. MS (EI): $m/z$ (%) = 206 (100) $[M]^+$. IR (neat): $\tilde{\nu}$ = 1707, 1634, 1580, 1559, 1516, 1473, 1450, 1391, 1368, 1359, 1301, 1278, 1237, 1227, 1211, 1169, 1146, 1115, 1089, 1067, 1032, 1016, 1001 $cm^{-1}$. HRMS (EI): calcd. for $C_{11}H_{10}O_3$ $[M]^+$ 206.0579; found 206.0580.

**2-(Ethoxycarbonyl)-5-styrylfuran (4h):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.3 mg, 0.2 mmol), MS (4 Å, 300.0 mg), **1n** (158.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 246.0 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (103.0 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (229.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4h** (149.6 mg, 62%) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.46 (d, $J$ = 7.2 Hz, 2 H, Ar-H), 7.37–7.21 (m, 4 H, Ar-H and CH=), 7.16 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.88 (d, $J$ = 16.5 Hz, 1 H, CH=), 6.41 (d, $J$ = 3.6 Hz, 1 H, CH=), 4.36 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 1.37 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 158.6, 156.6, 143.4, 136.0, 131.1, 128.6, 128.3, 126.6, 119.6, 115.3, 109.6, 60.7, 14.2 ppm. MS (EI): $m/z$ (%) = 242 (100) $[M]^+$. IR (neat): $\tilde{\nu}$ = 1708, 1570, 1506, 1446, 1383, 1367, 1294, 1257, 1225, 1196, 1131, 1016 $cm^{-1}$. HRMS (EI): calcd. for $C_{15}H_{14}O_3$ $[M]^+$ 242.0943; found 242.0945.

**2-(Ethoxycarbonyl)-5-(hex-1-en-1-yl)furan (4i):** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.4 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1o** (139.0 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.6 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (103.0 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $Cs_2CO_3$ (228.7 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4i** (143.0 mg, 64%) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.12 (d, $J$ = 3.3 Hz, 1 H, CH=), 6.45 (dt, $J_1$ = 15.8 Hz, $J_2$ = 7.0 Hz, 1 H, CH=), 6.27–6.18 (m, 2 H, 2 CH=), 4.34 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.20 (q, $J$ = 6.9 Hz, 2 H, $CH_2$), 1.51–1.24 (m, 7 H, 2 $CH_2$ and $CH_3$), 0.91 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 158.7, 156.9, 142.8, 135.0, 119.4, 117.8, 107.4, 60.6, 32.4, 30.8, 22.1, 14.2, 13.7 ppm. MS (EI): $m/z$ (%) = 222 (45.65) $[M]^+$, 166 (100). IR (neat): $\tilde{\nu}$ = 1714, 1655, 1577, 1504, 1465, 1382, 1298, 1207, 1138, 1115, 1016 $cm^{-1}$. HRMS (EI): calcd. for $C_{13}H_{18}O_3$ $[M]^+$ 222.1256; found 222.1258.

**Preparation of 2-(Ethoxycarbonyl)-5-(hex-1-en-1-yl)furan (4i) with $K_2CO_3$ as the Base:** By following the same procedure as that described for **4a**, the reaction of CuBr (98% purity, 29.5 mg, 0.2 mmol), MS (4 Å, 300.1 mg), **1o** (137.3 mg, 1.0 mmol) in dioxane (1.0 mL), ethyl glyoxalate (50% in toluene, 245.1 mg, 1.2 mmol) in dioxane (1.0 mL), and **2a** (102.7 mg, 1.2 mmol) in dioxane (1.0 mL) afforded the 2,5-dihydrofuran intermediate, which was treated with $K_2CO_3$ (97.0 mg, 0.7 mmol), $CH_3I$ ($d$ = 2.28 g/mL, 0.44 mL, 7.0 mmol), and $CH_3CN$ (4.0 mL) to give the crude product. Purification by column chromatography (petroleum ether/ethyl acetate, 200:1) afforded **4i** (128.4 mg, 58%) as a liquid. $^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ = 7.11 (d, $J$ = 3.6 Hz, 1 H, CH=), 6.45 (dt, $J_1$ = 15.7 Hz, $J_2$ = 7.0 Hz, 1 H, CH=), 6.27–6.18 (m, 2 H, 2 CH=), 4.35 (q, $J$ = 7.1 Hz, 2 H, $OCH_2$), 2.20 (q, $J$ = 7.2 Hz, 2 H, $CH_2$), 1.50–1.30 (m, 7 H, 2 $CH_2$ and $CH_3$), 0.91 (t, $J$ = 7.2 Hz, 3 H, $CH_3$) ppm. $^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ = 158.8, 156.9, 142.9, 135.0, 119.5, 117.8, 107.4, 60.6, 32.5, 30.9, 22.1, 14.3, 13.8 ppm.

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