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Base-Catalyzed Intramolecular 5-*exo*-*dig* Cyclization of 2-Propynyl-1,3-dicarbonyl Compounds: An Atom-Economic Route to Stereodefined 2-Methylene-2,3-dihydrofurans

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Keywords: Oxygen heterocycles / Spiro compounds / Alkynes / Cyclization / Intramolecular reactions / Base catalysis

A new and straightforward base-catalyzed 5-*exo*-*trig* cyclization of 2-propynyl-1,3-dicarbonyl compounds leads to the corresponding stereodefined 2-methylene-2,3-dihydrofurans in excellent yields.

Introduction

2,3-Dihydrofurans, an important class of oxygen heterocycles, are key structural components in many biologically active natural products and pharmaceuticals,[1] and they are also useful building blocks in organic synthesis.[2] Because of their importance, different approaches for the synthesis of 2,3-dihydrofuran derivatives have been developed. Substituted 2,3-dihydrofurans have been prepared mainly by two- or three-component intermolecular cyclization reactions.[3] Much less attention has been paid to atom-economic intramolecular heteroannulation reactions, even though it is also a straightforward and efficient strategy.[4] To date, only a few intramolecular approaches to the synthesis of 2,3-dihydrofurans are available, and they include: (1) the nickel-catalyzed rearrangement of 1-acyl-2-vinylcyclopropanes;[4a] (2) the electrophile-induced cyclization/1,2-migration of 2-alkynyl-2-silyloxy carbonyl compounds;[4b] and (3) the silver-catalyzed cyclization of *gem*-difluorohomopropargyl alcohols.[4c] The synthetic methods developed to date, however, have some drawbacks. For example, the starting materials may not be readily available, and the reactions may require transition-metal catalysts. As a result of the increased interest in these oxygen heterocycles, there is still demand for new methods that can enhance the efficiency of reactions and increase the variety of substituents. 2-Propynyl-1,3-dicarbonyl compounds are readily available, and the presence of carbonyl and alkynyl groups in the same molecule skeleton means that they are useful synthetic intermediates.[5] These compounds have been widely used for the synthesis of furans by intramolecular oxaannulation (Figure 1a).[6] However, reports regarding the chemoselective formation of 2,3-dihydrofurans are rarely found in the literature (Figure 1b).[7] Considering the easy availability of 2-propynyl-1,3-dicarbonyl compounds and the importance of 2,3-dihydrofurans, it would be very interesting to prepare 2,3-dihydrofurans starting from 2-propynyl-1,3-dicarbonyl compounds, especially under metal-free conditions.

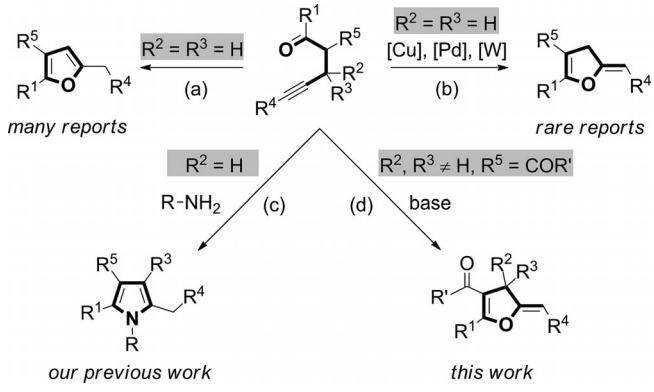

Figure 1. Regioselective intramolecular annulations of 2-propynyl-1,3-dicarbonyl compounds.

As part of our ongoing research into the development of new reactions using functionalized alkynes,[8] we previously reported a highly efficient iron-catalyzed [4C + 1N] annulation of 2-propynyl-1,3-dicarbonyl compounds with primary amines, which allowed the synthesis of a variety of tetrasubstituted and fully substituted pyrroles in good yields (Figure 1c).[8j] When we subjected 2-propynyl-1,3-dicarbonyl compounds containing a quaternary carbon center at the C-3 position (R^2, $R^3 \neq H$) to the base-catalyzed

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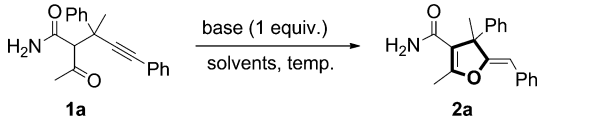
conditions, *cis*-2-methylene-2,3-dihydrofurans were formed stereoselectively in high to excellent yields (Figure 1d).[9] The key ring-closing step involves the regioselective 5-*exo-dig* annulation of the in-situ-generated oxygen anion with the alkyne group. In this paper, we describe this simple and atom-economic route to 2,3-dihydrofurans.

Results and Discussion

The reaction conditions were optimized using the reaction of model substrate **1a** with different bases and in different solvents, and the results are summarized in Table 1. With 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base, most of reactant **1a** was recovered when the reaction was run at 80 °C for 3 h in DMF, DCE (1,2-dichloroethane), or toluene (Table 1, Entries 1–3), but an excellent yield (92%) of dihydrofuran product **2a** was obtained using pentane-1,5-diol as the solvent (Table 1, Entry 4). Using ethylene glycol as the solvent resulted in a slightly lower yield (85%; Table 1, Entry 5). When the reaction temperature was increased from 80 to 100 °C, we were pleased to find that the reaction time was shortened to 30 min, and that the product was formed in 98% yield (Table 1, Entry 6). Other organic bases such as 1,4-diazabicyclo[2.2.2]octane (DABCO) and Et_3N were also examined, but no reaction took place (Table 1, Entries 7 and 8). Inorganic bases were also tested. With NaOH, the reaction did not go to completion (Table 1, Entry 9), whereas with Na_2CO_3 no reaction was observed (Table 1, Entry 10). Therefore, the conditions listed in Table 1, Entry 6 [i.e., DBU (1 equiv.), in pentane-1,5-diol at 100 °C] were found to be optimal, and these conditions were used in subsequent reactions.

Table 1. Optimization of reaction conditions.[a]



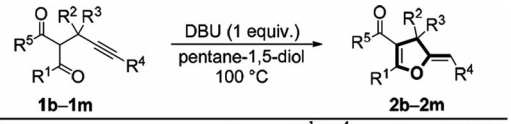
1a 2a

Entry	Base	Solvent	*T* [°C]	Time [min]	Yield [%][b]
1	DBU[d]	DMF[e]	80	180	51 (100)[c]
2	DBU	DCE[f]	80	180	57 (100)[c]
3	DBU	toluene	80	180	28 (100)[c]
4	DBU	pentane-1,5-diol	80	180	92
5	DBU	ethylene glycol	80	180	85
6	DBU	pentane-1,5-diol	100	30	98
7	DABCO[g]	pentane-1,5-diol	100	30	n.r.[h]
8	Et_3N	pentane-1,5-diol	100	30	n.r.[h]
9	NaOH	pentane-1,5-diol	100	30	100 (51)[c]
10	Na_2CO_3	pentane-1,5-diol	100	30	n.r.[h]

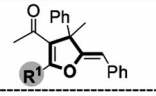
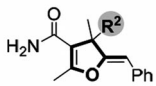
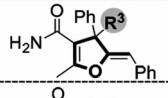
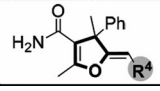
[a] Reactions were carried out with 2-propynyl-1,3-dicarbonyl compound **1a** (1.0 mmol) and base (1 equiv.) in solvent (2 mL). [b] Isolated yields. [c] The ratio of product **2a** to recovered starting material **1a** (in parentheses) was determined from analysis of the ^1H NMR spectrum of the crude reaction mixture. [d] DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene. [e] DMF = *N*,*N*-dimethylformamide. [f] DCE: 1,2-dichloroethane. [g] DABCO = 1,4-diazabicyclo[2.2.2]-octane. [h] n.r. = no reaction.

Having established the optimal reaction conditions, diverse 2-propynyl-1,3-dicarbonyl compounds (**1b**–**1m**) with varied functional groups (R^1–R^5) were tested in the cyclization reaction. As shown in Table 2, all the reactions smoothly proceeded to give the corresponding 2-methylene-2,3-dihydrofurans (i.e., **2b**–**2m**) in good to excellent yields (76–93%). We found that the reaction time was reduced to 10 min when R^1 was changed from an amino group (in **1a**) to an alkyl (Me; in **1b**), heteroaryl (2-thienyl; in **1c**), or aryl (Ph; in **1d**) group, and the corresponding 2,3-dihydrofurans (i.e., **2b**–**2d**) were produced in 86, 90, and 80% yields, respectively (Table 2, Entries 1–3). The electronic properties of the substituents at the quaternary carbon center affected the reaction outcome. For example, when the phenyl ring at R^2 was substituted with an electron-donating group, e.g., 4-MeO (Table 2, Entry 4), the corresponding product was formed in a slightly higher yield than when it was substituted with an electron-withdrawing substituent, e.g., 4-Cl (Table 2, Entry 5). The stereochemistry and the structure of the 2,3-dihydrofurans were unambiguously confirmed by the single-crystal X-ray diffraction analysis of product **2f** (Figure 2). As well as electronic effects, steric hindrance has a great influence on the reaction. When R^2 was a bulky 2-naphthyl group, the reaction time increased to 6 h, and the corresponding product was formed in 76% yield (Table 2, Entry 7). In contrast, the substrate in which R^2 was 2-thienyl gave the corresponding product (i.e., **2i**) in 87% yield within 50 min (Table 2, Entry 8). Interestingly, the substrate with an ethyl group as R^3 was found to require a much longer reaction time (240 min) than its phenyl-substituted counterpart (Table 2, Entries 9 and 10). The electronic properties of the R^4 substituent on the alkyne unit also had a dramatic influence on the reaction. For example, the reaction of compound **1l**, containing a 4-fluorophenyl group, finished within 15 min, whereas the reaction time for the

Table 2. Scope of the reaction.[a]



1b–1m 2b–2m

Entry		2	R^1–R^4	Time [min]	Yield [%][a]
1		**2b**	Me	10	86
2		**2c**	2-thienyl	10	90
3		**2d**	Ph	10	80
4		**2e**	4-$MeOC_6H_4$	30	92
5		**2f**	4-ClC_6H_4	30	82
6		**2g**	3-ClC_6H_4	30	80
7		**2h**	2-naphthyl	360	76
8		**2i**	2-thienyl	50	87
9		**2j**	Ph	30	88
10		**2k**	Et	240	81
11		**2l**	4-FC_6H_4	15	93
12		**2m**	4-MeC_6H_4	240	88

[a] Isolated yields.

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substrate **1m**, bearing a *p*-methylphenyl group, was as long as 240 min (Table 2, Entries 11 and 12). The formation of only the *cis* isomer of compounds **2** may be ascribed to the steric hindrance and van der Waals repulsion between the R^4 and R^2/R^3.

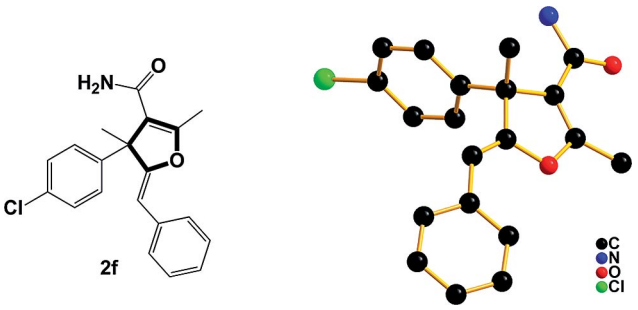
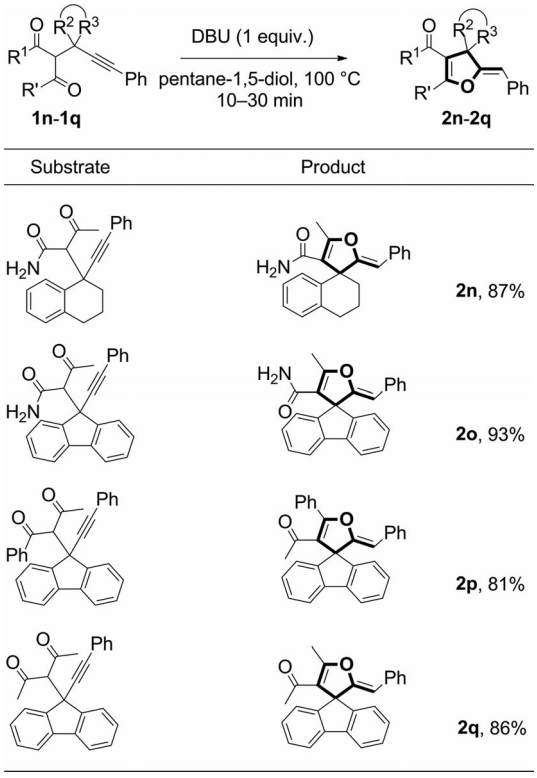


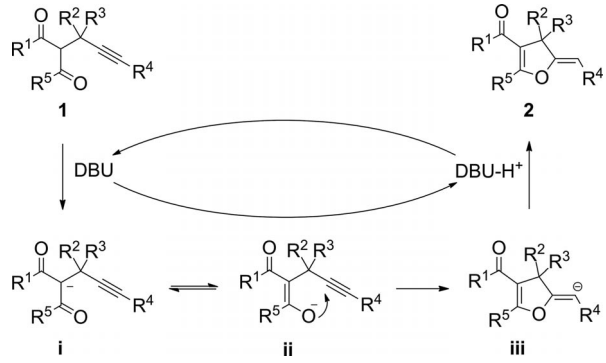
Figure 2. X-ray crystal structure of compound **2f**.

The spiro-dihydrofuran skeleton has been found in several biologically active natural products, including phelligridin G, and pleurospiroketals A–E.[10] Therefore, the development of efficient synthetic routes to the spiro-dihydrofuran skeleton would be very valuable. However, methods for the synthesis of spiro-dihydrofurans remain rare. Recently, Shaabani and co-workers reported a facile three-component reaction between benzo[*b*]acridine-6,11-dione, an electron-deficient acetylene compound, and an isocyanide that led to the formation of spiro-benzo[*b*]-acridine-furans.[11] Since cyclic-ketone-derived 2-propynyl-1,3-dicarbonyl compounds **1n**–**1q** could easily be prepared through the intermolecular dehydration coupling of tertiary propargyl alcohols and 1,3-dicarbonyl compounds, we envisaged that **1n**–**1q** could be suitable substrates for this intramolecular regio- and stereoselective 5-*exo*-*dig* cyclization reaction, which would lead to spiro-dihydrofurans. To this end, we subjected substrates **1n**–**1q** to the base-catalyzed procedure (Scheme 1). We were pleased to find that the reactions proceeded smoothly in all cases to give the corresponding spiro-dihydrofuran products (i.e., **2n**–**2q**) in excellent yields (81–93%). The regioselectivity in the formation of product **2p**, i.e., reacting at the benzoyl group rather than the acetyl group, was confirmed by HMBC spectral analysis. It is worth noting that these reactions also produced *cis*-configured products stereoselectively.



Scheme 1. Synthesis of spiro-dihydrofurans.

On the basis of these experimental results and related precedent,[6,7] a plausible mechanism for this 5-*exo*-*dig* cyclization reaction is proposed (Scheme 2). First, a proton is removed from substrate **1** by DBU to give intermediate **i**. Subsequently, enol anion **ii** is generated by keto/enol tautomerism. Following regioselective addition of the oxygen anion to the carbon–carbon triple bond of the alkynyl unit, an olefinic carbanion intermediate **iii** is formed. Finally, 2-methylene-2,3-dihydrofuran **2** is obtained by protonation, and DBU is regenerated for the next reaction.



Scheme 2. Plausible reaction mechanism.

Conclusions

A new and efficient intramolecular regioselective cyclization of easily available 2-propynyl-1,3-dicarbonyl compounds has been developed. This reaction constitutes a new and straightforward route to stereodefined 2-methylene-2,3-dihydrofurans. The advantages of this reaction include an operationally simple procedure, excellent yields of the products, short reaction times, and a good functional-group tolerance. Efforts to extend the scope of this method are ongoing in our laboratory.

Experimental Section

General Remarks: All reagents were purchased from commercial suppliers, and were used without treatment unless otherwise indicated. Products were purified by column chromatography on silica gel. ^{1}H and ^{13}C NMR spectra were recorded at 25 °C with a Varian instrument at 500 and 125 MHz, respectively, and tetramethylsilane was used as an internal standard. High-resolution mass spectra

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(HRMS) were recorded with a Bruker microTOF instrument using the ESI method. CCDC-1011307 (for **2f**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Typical Synthetic Procedure (with 2a as an example): Compound **1a** (1 mmol, 305.1 mg) and DBU (149.4 μL, 1 mmol) were added to pentane-1,5-diol (2.0 mL) while stirring. The mixture was warmed to 100 °C and stirred for 30 min. When TLC showed that the starting material had been consumed, the reaction mixture was poured into saturated aqueous sodium chloride (5 mL). The mixture was extracted with dichloromethane (3 × 5 mL), and the combined organic extracts were washed with water (3 × 5 mL), dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (silica gel, petroleum ether/ethyl acetate, 10:4) to give **2a** (299.0 mg, 98%) as a white solid.

(*Z*)-5-Benzylidene-2,4-dimethyl-4-phenyl-4,5-dihydrofuran-3-carboxamide (2a): White solid. m.p. 138–140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.85 (s, 3 H), 2.54 (s, 3 H), 4.76 (s, 1 H), 5.10 (s, 1 H), 5.81 (s, 1 H), 7.11–7.14 (m, 1 H), 7.24–7.30 (m, 3 H), 7.35–7.41 (m, 4 H), 7.46 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 26.0, 53.8, 102.1, 114.8, 126.0, 126.6, 127.7, 127.9, 128.2, 129.1, 134.7, 143.7, 163.3, 163.6, 166.2 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{20}NO_2$ [M + H]$^+$ 306.1494; found 306.1487.

(*Z*)-1-(5-Benzylidene-2,4-dimethyl-4-phenyl-4,5-dihydrofuran-3-yl)-ethanone (2b): White solid. m.p. 98–100 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.90 (s, 3 H), 1.93 (s, 3 H), 2.55 (s, 3 H), 5.17 (s, 1 H), 7.12–7.15 (m, 1 H), 7.20–7.24 (m, 1 H), 7.26–7.30 (m, 2 H), 7.31–7.36 (m, 6 H), 7.47–7.49 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2, 26.5, 29.8, 54.1, 102.4, 123.1, 126.1, 126.3, 126.7, 127.9, 128.2, 128.4, 134.7, 144.8, 163.8, 164.7, 193.9 ppm. HRMS (ESI-TOF): calcd. for $C_{21}H_{21}O_2$ [M + H]$^+$ 305.1542; found 305.1545.

(*Z*)-1-[5-Benzylidene-4-methyl-4-phenyl-2-(thiophen-2-yl)-4,5-dihydrofuran-3-yl]ethanone (2c): White solid. m.p. 169–171 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.02 (s, 3 H), 2.17 (s, 3 H), 5.26 (s, 1 H), 7.03–7.04 (m, 1 H), 7.15–7.19 (m, 2 H), 7.23–7.32 (m, 4 H), 7.42–7.44 (m, 3 H), 7.54–7.57 (m, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.5, 26.8, 57.0, 102.1, 122.5, 126.1, 126.5, 126.7, 127.5, 128.0, 128.2, 128.3, 132.5, 133.2, 134.9, 144.3, 145.6, 159.7, 163.8, 183.6 ppm. HRMS (ESI-TOF): calcd. for $C_{24}H_{21}O_2S$ [M + H]$^+$ 373.1262; found 373.1264.

(*Z*)-1-(5-Benzylidene-4-methyl-2,4-diphenyl-4,5-dihydrofuran-3-yl)-ethanone (2d): Yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.85 (s, 3 H), 2.03 (s, 3 H), 5.28 (s, 1 H), 7.13–7.15 (m, 1 H), 7.21–7.23 (m, 1 H), 7.25–7.29 (m, 2 H), 7.32–7.35 (m, 2 H), 7.44 (d, J = 8.0 Hz, 2 H), 7.50–7.57 (m, 5 H), 7.71–7.73 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.3, 30.2, 56.2, 102.6, 124.4, 126.1, 126.3, 126.7, 128.0, 128.2, 128.3, 128.6, 129.4, 129.9, 131.0, 134.8, 144.8, 162.2, 163.6, 194.2 ppm. HRMS (ESI-TOF): calcd. for $C_{26}H_{23}O_2$ [M + H]$^+$ 367.1698; found 367.1739.

(*Z*)-5-Benzylidene-4-(4-methoxyphenyl)-2,4-dimethyl-4,5-dihydrofuran-3-carboxamide (2e): White solid. m.p. 185–183 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.82 (s, 3 H), 2.53 (s, 3 H), 3.80 (s, 3 H), 4.84 (s, 1 H), 5.09 (s, 1 H), 5.81 (s, 1 H), 6.89 (d, J = 7.5 Hz, 2 H), 7.12–7.15 (m, 1 H), 7.25–7.30 (m, 2 H), 7.30–7.34 (m, 2 H), 7.47 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 26.3, 53.3, 55.2, 101.8, 114.4, 114.7, 126.0, 127.8, 127.9, 128.3, 134.8, 135.6, 158.9, 163.1, 163.9, 166.3 ppm. HRMS (ESI-TOF): calcd. for $C_{21}H_{22}NO_3$ [M + H]$^+$ 336.1600; found 336.1583.

(*Z*)-5-Benzylidene-4-(4-chlorophenyl)-2,4-dimethyl-4,5-dihydrofuran-3-carboxamide (2f): Yellow solid. m.p. 206–208 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.84 (s, 3 H), 2.54 (s, 3 H), 4.74 (s, 1 H), 5.08 (s, 1 H), 5.89 (s, 1 H), 7.13–7.16 (m, 1 H), 7.25–7.30 (m, 2 H), 7.32–7.37 (m, 4 H), 7.46 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 26.2, 53.5, 102.5, 114.4, 126.3, 127.9, 128.0, 128.3, 129.3, 133.7, 134.4, 142.4, 163.0, 163.6, 165.9 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{19}ClNO_2$ [M + H]$^+$ 340.1104; found 340.1108.

(*Z*)-5-Benzylidene-4-(3-chlorophenyl)-2,4-dimethyl-4,5-dihydrofuran-3-carboxamide (2g): White solid. m.p. 140–142 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.85 (s, 3 H), 2.56 (s, 3 H), 4.73 (s, 1 H), 5.11 (s, 1 H), 5.73 (s, 1 H), 7.14–7.17 (m, 1 H), 7.25–7.34 (m, 5 H), 7.39–7.40 (m, 1 H), 7.47–7.49 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 26.1, 53.7, 102.6, 114.3, 124.8, 126.3, 126.7, 127.9, 128.3, 130.5, 134.4, 135.1, 146.0, 162.7, 163.9, 165.7 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{19}ClNO_2$ [M + H]$^+$ 340.1104; found 340.1093.

(*Z*)-5-Benzylidene-2,4-dimethyl-4-(naphthalen-2-yl)-4,5-dihydrofuran-3-carboxamide (2h): Yellow solid. m.p. 221–223 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.97 (s, 3 H), 2.57 (s, 3 H), 4.82 (s, 1 H), 5.10 (s, 1 H), 5.72 (s, 1 H), 7.11–7.14 (m, 1 H), 7.23–7.27 (m, 2 H), 7.36–7.37 (m, 1 H), 7.45 (d, J = 7.5 Hz, 2 H), 7.50–7.56 (m, 2 H), 7.79–7.83 (m, 2 H), 7.88 (d, J = 8.0 Hz, 1 H), 7.93 (s, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 26.1, 54.1, 102.5, 114.4, 123.8, 125.8, 126.1, 126.6, 126.7, 127.6, 127.9, 128.0, 128.3, 129.3, 132.5, 133.0, 134.6, 141.1, 163.2, 163.7, 166.1 ppm. HRMS (ESI-TOF): calcd. for $C_{24}H_{22}NO_2$ [M + H]$^+$ 356.1651; found 356.1640.

(*Z*)-5-Benzylidene-2,4-dimethyl-4-(thiophen-2-yl)-4,5-dihydrofuran-3-carboxamide (2i): White solid. m.p. 244–146 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.90 (s, 3 H), 2.52 (s, 3 H), 5.15 (s, 1 H), 5.31 (s, 1 H), 5.93 (s, 1 H), 6.97–6.99 (m, 1 H), 7.06–7.09 (m, 1 H), 7.14–7.17 (m, 1 H), 7.27–7.31 (m, 3 H), 7.50 (d, J = 8.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 27.8, 51.7, 102.3, 114.1, 124.5, 126.3, 126.7, 126.9, 128.1, 128.3, 134.5, 149.5, 162.1, 163.6, 166.0 ppm. HRMS (ESI-TOF): calcd. for $C_{18}H_{18}NO_2S$ [M + H]$^+$ 312.1058; found 312.1044.

(*Z*)-5-Benzylidene-2-methyl-4,4-diphenyl-4,5-dihydrofuran-3-carboxamide (2j): White solid. m.p. 258–260 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.55 (s, 3 H), 5.03 (s, 1 H), 5.40 (s, 1 H), 5.61 (s, 1 H), 7.15–7.18 (m, 1 H), 7.28–7.32 (m, 4 H), 7.35–7.38 (m, 4 H), 7.44–7.48 (m, 4 H), 7.51 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.4, 64.3, 106.0, 113.5, 126.5, 127.6, 128.3, 128.4, 128.67, 128.69, 134.5, 142.7, 162.8, 163.7, 166.4 ppm. HRMS (ESI-TOF): calcd. for $C_{25}H_{22}NO_2$ [M + H]$^+$ 368.1651; found 368.1655.

(*Z*)-5-Benzylidene-4-ethyl-2-methyl-4-phenyl-4,5-dihydrofuran-3-carboxamide (2k): White solid. m.p. 175–177 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (t, J = 7.5 Hz, 3 H), 2.08–2.14 (m, 1 H), 2.35–2.43 (m, 1 H), 2.56 (s, 3 H), 4.75 (s, 1 H), 5.08 (s, 1 H), 5.94 (s, 1 H), 7.13 (t, J = 7.5 Hz, 1 H), 7.24–7.29 (m, 3 H), 7.36 (t, J = 7.5 Hz, 2 H), 7.40–7.43 (m, 2 H), 7.47 (d, J = 7.0 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 9.0, 13.9, 30.5, 58.7, 102.4 111.5 126.1 126.6, 127.6, 127.9, 128.2, 129.1, 134.8 144.3 161.9, 163.9, 166.2 ppm. HRMS (ESI-TOF): calcd. for $C_{21}H_{22}NO_2$ [M + H]$^+$ 320.1651; found 320.1654.

(*Z*)-5-(4-Fluorobenzylidene)-2,4-dimethyl-4-phenyl-4,5-dihydrofuran-3-carboxamide (2l): White solid. m.p. 242–244 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.85 (s, 3 H), 2.55 (s, 3 H), 4.75 (s, 1 H), 5.06 (s, 1 H), 5.53 (s, 1 H), 6.94–6.98 (m, 2 H), 7.29–7.32 (m, 1 H), 7.37–7.45 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.0, 26.1, 53.8, 101.1, 114.8, 115.0 (d, J = 21.0 Hz), 126.6, 127.8, 129.2, 129.4 (d, J = 8.0 Hz), 130.9 (d, J = 3.0 Hz), 143.7, 160.0, 162.0, 163.1, 163.18, 163.20, 163.4, 166.0 ppm. HRMS (ESI-TOF): calcd. for $C_{20}H_{19}FNO_2$ [M + H]$^+$ 324.1400; found 324.1398.

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(*Z*)-2,4-Dimethyl-5-(4-methylbenzylidene)-4-phenyl-4,5-dihydrofuran-3-carboxamide (2m): White solid. m.p. 240–242 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.84 (s, 3 H), 2.30 (s, 3 H), 2.54 (s, 3 H), 4.75 (s, 1 H), 5.07 (s, 1 H), 5.59 (s, 1 H), 7.08 (d, J = 8.0 Hz, 2 H), 7.28–7.31 (m, 1 H), 7.35–7.40 (m, 4 H), 7.40–7.43 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.1, 21.1, 26.2, 53.7, 102.1, 114.6, 126.6, 127.6, 127.8, 129.0, 129.1, 131.8, 135.8, 143.9, 162.9, 163.5, 166.2 ppm. HRMS (ESI-TOF): calcd. for $C_{21}H_{22}NO_2$ [M + H]$^+$ 320.1651; found 320.1643.

(*Z*)-2-Benzylidene-5-methyl-3′,4′-dihydro-2*H*,2′*H*-spiro[furan-3,1′-naphthalene]-4-carboxamide (2n): White solid. m.p. 254–256 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.87–1.89 (m, 1 H), 2.01–2.06 (m, 1 H), 2.14–2.22 (m, 2 H), 2.55 (s, 3 H), 2.80–2.87 (m, 1 H), 2.90–2.97 (m, 1 H), 4.66 (s, 1 H), 5.07 (s, 1 H), 5.32 (s, 1 H), 7.13–7.22 (m, 5 H), 7.26–7.30 (m, 2 H), 7.47–7.50 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 17.3, 29.2, 35.4, 53.9, 104.4, 114.4, 126.2, 127.2, 127.6, 128.1, 128.3, 129.6, 130.1, 134.7, 137.2, 137.5, 163.95, 163.97, 166.0 ppm. HRMS (ESI-TOF): calcd. for $C_{22}H_{22}NO_2$ [M + H]$^+$ 332.1651; found 332.1645.

(*Z*)-2′-Benzylidene-5′-methyl-2′*H*-spiro[fluorene-9,3′-furan]-4′-carboxamide (2o): Pale yellow solid. m.p. 275–277 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.68 (s, 3 H), 4.21 (s, 1 H), 4.74, (s, 1 H), 5.24 (s, 1 H), 7.09–7.12 (m, 1 H), 7.21–7.24 (m, 2 H), 7.29–7.35 (m, 2 H), 7.35–7.41 (m, 4 H), 7.41–7.44 (m, 2 H), 7.78 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.4, 64.1, 102.3, 110.1, 120.5, 125.0, 126.3, 128.1, 128.2, 128.88, 128.92, 134.3, 139.4, 148.1, 157.6, 165.1, 166.8 ppm. HRMS (ESI-TOF): calcd. for $C_{25}H_{20}NO_2$ [M + H]$^+$ 366.1494; found 366.1022.

(*Z*)-1-(2′-Benzylidene-5′-phenyl-2′*H*-spiro[fluorene-9,3′-furan]-4′-yl)ethanone (2p): White solid. m.p. 221–223 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.56 (s, 3 H), 4.86 (s, 1 H), 7.12–7.13 (m, 1 H), 7.22–7.25 (m, 2 H), 7.32–7.35 (m, 2 H), 7.42–7.44 (m, 6 H), 7.54–7.58 (m, 3 H), 7.81 (d, J = 7.0 Hz, 2 H), 7.95–7.99 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.9, 65.6, 102.9, 118.9, 120.4, 124.2, 126.4, 128.2, 128.3, 128.4, 128.5, 129.3, 129.5, 131.3, 134.3, 140.4, 149.1, 157.4, 164.5, 193.5 ppm. HRMS (ESI-TOF): calcd. for $C_{31}H_{23}O_2$ ([M + H]$^+$) 427.1699; found 427.1695.

(*Z*)-1-(2′-Benzylidene-5′-methyl-2′*H*-spiro[fluorene-9,3′-furan]-4′-yl)ethanone (2q): White solid. m.p. 212–214 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.20 (s, 3 H), 2.71 (s, 3 H), 4.78 (s, 1 H), 7.10–7.13 (m, 1 H), 7.22–7.25 (m, 2 H), 7.31–7.32 (m, 4 H), 7.39–7.45 (m, 4 H), 7.79 (d, J = 7.5 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 15.2, 28.1, 64.0, 102.6, 117.7, 120.3, 124.5, 126.4, 128.21, 128.23, 128.5, 134.3, 140.2, 149.0, 157.9, 168.1, 194.8 ppm. HRMS (ESI-TOF): calcd. for $C_{26}H_{21}O_2$ [M + H]$^+$ 365.1542; found 365.1533.

Supporting Information (see footnote on the first page of this article): Crystallographic data for compound **2f**; copies of ^{1}H and ^{13}C NMR spectra; HMBC spectra of **2b** and **2q**.

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