JOC The Journal of Organic Chemistry

Article

Regioselective and Stereoselective Pd-catalyzed Intramolecular Arylation of Furans: Access to Spirooxindoles and 5H-Furo[2,3-c]quinolin-4-ones

Jianchao Liu, Hui Peng, Yongjie Yang, Huanfeng Jiang, and Biaolin Yin

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.6b01774 • Publication Date (Web): 23 Sep 2016

Just Accepted

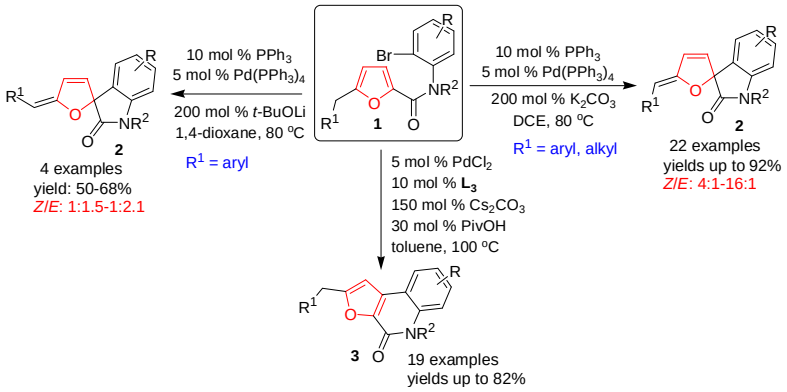
ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Regioselective and Stereoselective Pd-catalyzed Intramolecular Arylation of Furans: Access to Spirooxindoles and 5*H*-Furo[2,3-*c*]quinolin-4-ones

Jianchao Liu, Hui Peng, Yongjie Yang, Huanfeng Jiang and Biaolin Yin*

Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510640, P. R. China 510640



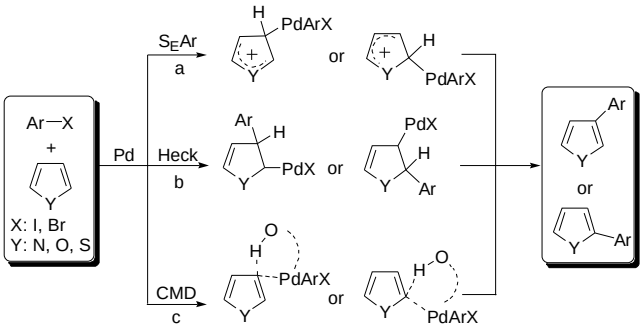
Abstract: Herein, we report regio- and stereoselective intramolecular direct arylations of *N*-(2-bromophenyl)-2-furancarboxamides **1** to produce spirooxindoles **2** and 5*H*-furo[2,3-*c*]quinolin-4-ones **3** under different reaction conditions. Specifically, in the presence of $Pd(PPh_3)_4$ as a catalyst, PPh_3 as a ligand, and K_2CO_3 as a base, substrates **1** underwent intramolecular α-arylation, possibly via a Heck insertion pathway, to provide **2**, with the *Z*-isomer being favored. When the base was *t*-BuOLi and R^1 was an aryl group, the reaction favored *E*-**2**, possibly via an electrophilic palladation pathway. In contrast, in the presence of $PdCl_2$ as a catalyst, (*o*-OMePh)$_3$P as a ligand, and PivOH as an additive, substrates **1** underwent intramolecular β-arylation to provide **3**, possibly via a concerted metalation–deprotonation process.

INTRODUCTION

The synthesis of bi(hetero)aryl compounds, which have interesting bioactivities[1] and physical

properties,[2] by means of direct arylation of five-membered heteroaromatic rings (such as furans, pyrroles, and thiophenes) is an important but challenging task in organic synthesis.[3] Three major reaction pathways involving palladium catalysis have been proposed for this transformation (Scheme 1). One commonly proposed pathway for reaction of π-electron-rich aromatic substrates is electrophilic aromatic substitution (S_EAr),[4] whereby an ArPdX intermediate attacks at the most electronegative position of the heteroaromatic substrate (Scheme 1a). A Heck-type pathway involving β-H elimination[5] (Scheme 1b) and a concerted metalation–deprotonation (CMD) process[6] have also been suggested (Scheme 1c). Recently, several groups have reported the regioselective direct arylation of five-membered heteroaromatic rings by means of elegant methods involving the use of different reaction conditions to alter the reaction pathway.[7] For example, Sharp and co-workers[5a] regioselectively arylated 3-furoate and 3-thiophenecarboxylate esters with aryl bromides and could change the reaction pathway by varying the palladium source and the solvent. Doucet[7a] reported that the regioselectivity of the arylation of 2,5-disubstituted furans depended strongly on the base that was used.

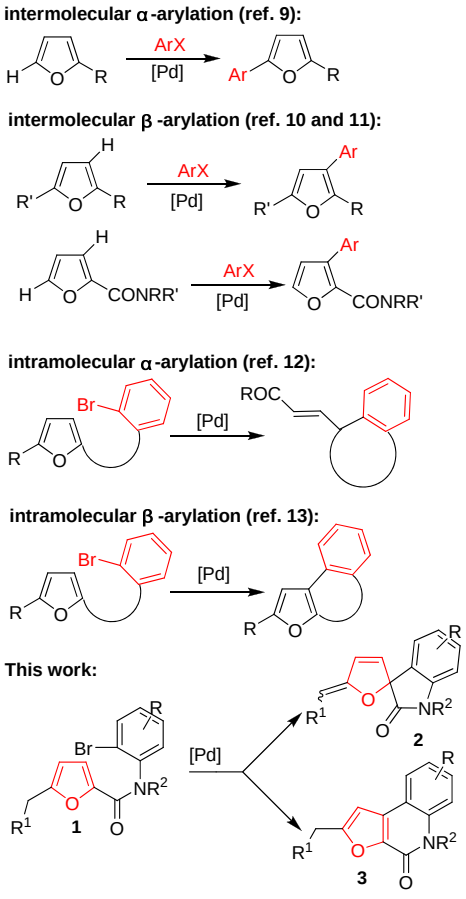
Scheme 1. Major Pathways for Direct Arylation of Five-Membered Heteroaromatic Rings



Biomass derived α-substituted furans are readily available and are excellent, widely used building blocks for the construction of complex molecules.[8] Direct arylation is an important tool for transforming α-substituted furans into other useful compounds (Scheme 2). Intermolecular

arylation of α-monosubstituted furans generally occurs at the unsubstituted α-position.[9] Intermolecular β-arylation of furans occurs only when both of the α-positions are substituted[10] or when a 2-furancarboxamide is used as the substrate; the latter reaction involves chelation-assisted functionalization of the *ortho*-C–H bonds, directed by the amide group.[11] Intramolecular α-arylation of α-substituted furans usually leads to opening of the furan ring to form α,β-unsaturated carbonyl compounds.[12] Intramolecular β-arylation of α-furans has also been reported to afford annulated furans.[13]

Scheme 2. α and β-Arylation of α-Substituted Furans



Although numerous elegant methods for arylation of α-substituted furans have been reported and used to extend the synthetic applications of furans, tuning the regio- and stereoselectivities of furan arylation reactions by altering the reaction pathway by means of different reaction conditions has not

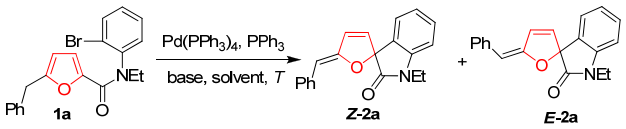
yet been reported. As part of our ongoing work on furan dearomatization and palladium catalysis,[14] in this study, we carried out regio- and stereoselective intramolecular arylation reactions of furans by using readily available *N*-(2-bromophenyl)-2-furancarboxamides **1** as the substrates (Scheme 2). These reactions afforded biologically interesting spirooxindoles **2**[15] or *5H*-furo[2,3-c]quinolin-4-ones **3**[16] depending on the reaction conditions, and the reactions probably proceeded by three different pathways.

RESULTS AND DISCUSSION

We used 2-furancarboxamide **1a** as the substrate for optimization of the reaction conditions (Table 1). When **1a** was treated with $Pd(PPh_3)_4$ (5 mol %), PPh_3 (10 mol %) and K_2CO_3 (200 mol %) in 1,4-dioxane at 80 °C under nitrogen for 12 h, α-arylated spirooxindole **2a** was obtained in 93% yield as a 6:1 *Z*/*E* mixture (entry 1). The stereochemistry of **2a** was assigned by means of NOESY experiments (see the ESI). The reaction did not occur in the absence of $Pd(PPh_3)_4$ (entry 2), and only a trace of **2a** was produced in the absence of a base (entry 3). Screening of a series of other bases revealed that the base clearly influenced the outcome of the reaction (entries 4–10). Among the weak bases, Na_2CO_3 gave **2a** in a yield (90%) and a *Z*/*E* ratio (5.8:1) that were comparable to those observed with K_2CO_3 (entry 4). The use of Cs_2CO_3 and DBU led to lower yields and *Z*/*E* ratios than K_2CO_3 (entries 5 and 6). Li_2CO_3 gave only a trace of **2a** (entry 7). Notably, strong bases (*t*-BuOLi, *t*-BuONa, and *t*-BuOK) gave **2a** in low yields but with stereoselectivities opposite to that observed with the weak bases; that is, the *E*-isomer was the major isomer (entries 8–10). Among these strong bases, *t*-BuOLi gave the highest yield (55%) and the lowest *Z*/*E* ratio (1/2.7) (entry 8). On the basis of these results, we used K_2CO_3 or *t*-BuOLi as the base to favor the synthesis of the *Z*- or *E*-isomer of **2a**, respectively. Solvent screening demonstrated that DCE was optimal when K_2CO_3 was the base (entry 12), whereas 1,4-dioxane was

optimal for *t*-BuOLi (entry 8).

Table 1. Optimization of the α-Arylation of 1a[a]



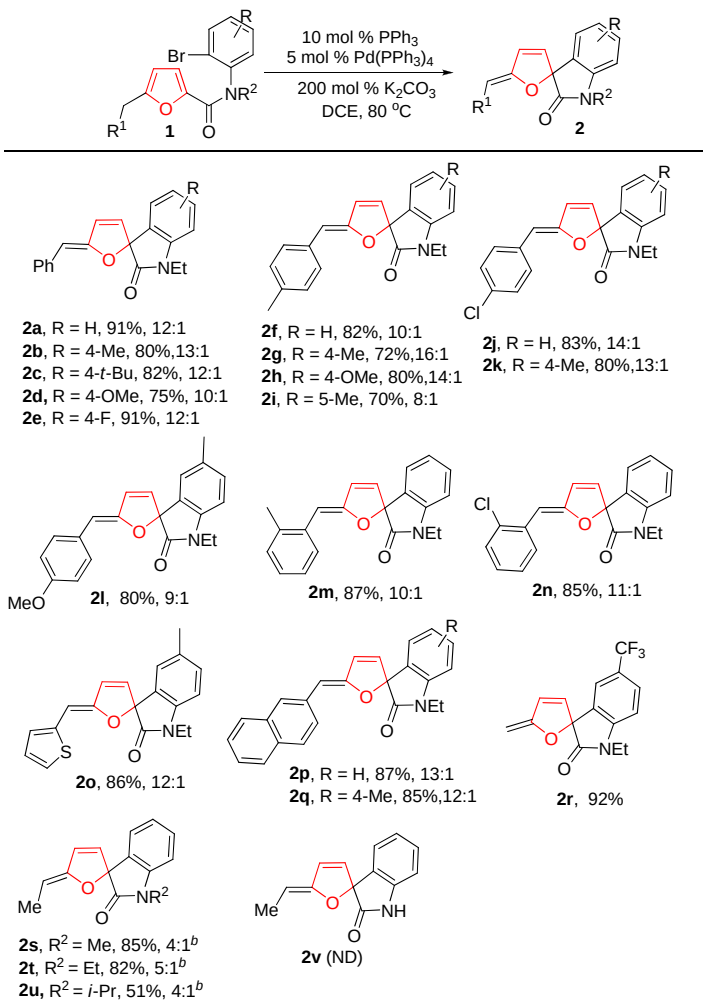
entry	base	solvent	yield of **2a** (%)[b]	Z/E[b]
1	K_2CO_3	1,4-dioxane	93	6/1
2[c]	K_2CO_3	1,4-dioxane	NR	—
3	—	1,4-dioxane	trace	—
4	Na_2CO_3	1,4-dioxane	90	5.8/1
5	Cs_2CO_3	1,4-dioxane	48	5/1
6	DBU	1,4-dioxane	35	1/1
7	Li_2CO_3	1,4-dioxane	trace	—
8	*t*-BuOLi	1,4-dioxane	53	1/2.7
9	*t*-BuONa	1,4-dioxane	45	1/2.5
10	*t*-BuOK	1,4-dioxane	52	1/1.5
11	K_2CO_3	toluene	97	4.8/1
12	K_2CO_3	DCE	98	12.5/1
13	K_2CO_3	THF	80	2.6/1
14	K_2CO_3	DMF	70	2.8/1
15	*t*-BuOLi	toluene	50	1/2
16	*t*-BuOLi	DCE	55	1/1.2
17	*t*-BuOLi	THF	60	1.3/1
18	*t*-BuOLi	DMF	37	1/1.2

[a]Reaction conditions, unless otherwise noted: **1a** (0.3 mmol), $Pd(PPh_3)_4$ (5 mol %), PPh_3 (10 mol %), base (200 mol %), solvent (3 mL), *T* = 80 °C, N_2 atmosphere, 12 h. NR = no reaction; ND = not detected. [b]Yields and *Z*/*E* ratios were determined by ^1H NMR analysis with mesitylene as an internal standard. [c]This reaction was carried out in the absence of $Pd(PPh_3)_4$.

To investigate the scope of the reaction, we subjected various *N*-(2-bromophenyl)-2-furancarboxamides **1** with different R, R^1, and R^2 groups to the optimized reaction conditions (Table 1, entry 12) to synthesize a range of spirooxindoles **2**, with the *Z*-isomer as the major product (Table 2). The reaction had a broad substrate scope, and in most cases, expected spirooxindoles **2** were obtained in good to excellent yields (51–92%) and good *Z*/*E* selectivities (4:1–16:1). Specifically, R could be an H atom, an electron-donating group (Me, *t*-Bu, OMe), or an

electron-withdrawing group (F). The R^1 substituent could be an alkyl group, a phenyl group (either unsubstituted or with an electron-donating or electron-withdrawing substituent), a thiophenyl group, or a naphthyl group. Notably, when R^1 was Me, the *Z*/*E* selectivities were lower (**2s**–**2u**) than those observed with other R^1 groups. The R^2 substituent could be a small alkyl group (Me, Et) or a slightly larger alkyl group (*i*-Pr), but when R^2 was H (**1v**), *O*-arylation occurred and the corresponding spirooxindole (**2v**) could not be isolated.

Table 2. Scope of the α-Arylation Reaction[a]

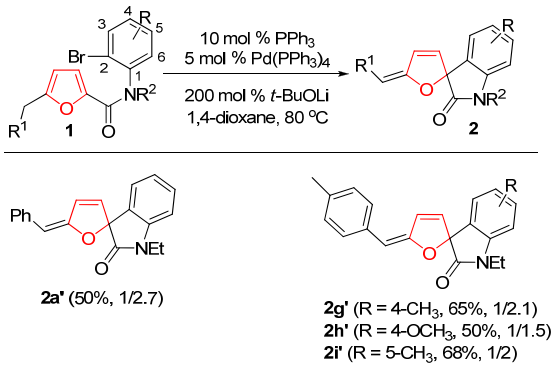


[a]Reaction conditions, unless otherwise noted: **1** (0.3 mmol), DCE (3 mL), T = 80 °C, under N_2, 12 h. Yields are isolated yields. *Z*/*E* ratios were determined by ^{1}H NMR analysis. ND = not detected. [b]T = 90 °C .

When **1a** (R^1 = Ph) and **1g-1h** (R^1 = *p*-Toly) were subjected to the reaction conditions listed in

entry 8 of Table 1, these substrates were transformed to corresponding products **2** in moderate isolated yields, with the *E*-isomer being favored (*Z*/*E* = 1:1.5–1:2.7, Scheme 3). Notably, when the substrate was **1s** (R^1 = Me), the product **2s'** was formed still with the *Z*-isomer being favored.

Scheme 3. Synthesis of *E*-isomers of 2a and 2g–2h[a]

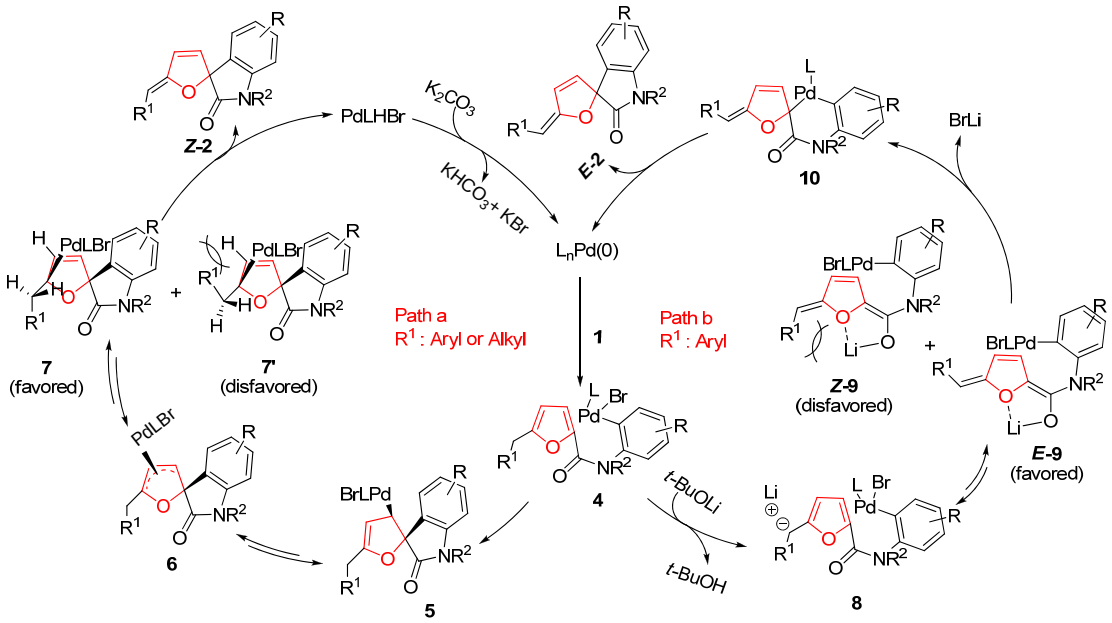


[a]Reaction conditions: **1** (0.3 mmol), 1,4-dioxane (3 mL), under N_2, 12 h. Yields are isolated yields. *Z*/*E* ratios were determined by ^{1}H NMR analysis.

In explanation of the stereoselectivity for the formation of **2** under the two different sets of reaction conditions, we propose the two paths shown in Scheme 4. The first step is oxidative addition of Pd(0) to **1** to produce palladium complex **4**. In the presence of K_2CO_3 (path a), **4** undergoes a Heck-type α-arylation of the furan ring to produce alkyl palladium **5**. Alkyl palladium **5** isomerizes to allylic palladium **6** and then to alkyl palladium **7** and **7′**, which undergo β-H elimination to form **2**.[17] The formation of **7** is favored, owing to the absence of an interaction between the olefinic proton and the phenyl group, and as a result, *Z*-**2** is the major. In contrast, when R^1 is an aryl group and *t*-BuOLi is used as the base (path b), deprotonation of the methylene carbon of **4** leads to carbanion **8**, which then undergoes a 1,7-lithium shift to form chelation complexes *Z*-**9** and *E*-**9**.[18] Complexes **9** undergo electrophilic palladation to produce **10**, and subsequent reductive elimination affords **2**. Complex *E*-**9** is favored over *Z*-**9** owing to the lack of an interaction between the phenyl group and the lithium salt, and

as a result, *E*-**2** is the major product. When R^1 is a methyl group, due to low acidity of the proton of the methylene carbon, the deprotonation of **4s** by *t*-BuOLi to **8s** is suppressed, thus **2s'** is formed through Heck-type insertion still with the *Z*-isomer as the major product.

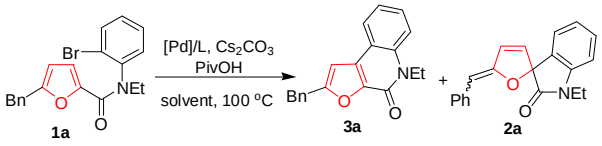
Scheme 4. Proposed Mechanisms for Formation of 2 under Different Reaction Conditions



Having investigated dearomatizing α-arylation of **1** to form spirooxindoles **2**, we next searched for suitable conditions to achieve intramolecular β-arylation to form β-arylated products **3** by suppressing α-arylation and enhancing the acidity of the β-H. Addition of a protonic acid, such as pivalic acid (PivOH), is known to increase the acidity of C–H protons during transformations involving C–H functionalization.[19] Thus, we set out to optimize the reaction conditions for the formation of **3** from substrate **1a** by using PivOH as an additive (Table 3). With $Pd(OAc)_2$ as the catalyst, $PCy_3{\cdot}HBF_4$ as the ligand, and Cs_2CO_3 as the base, reaction of **1a** at 100 °C in toluene provided **3a** and **2a** in 58% and 30% yields, respectively (entry 1). In the absence of PivOH, **2a** was the only product (85% yield, entry 2). Solvent screening demonstrated that toluene was optimal for the formation of **3a** (entries 3–8). Various ligands were then examined, and the ligand was found to strongly influence the reaction

outcome (entries 9–13). The electron-rich phenyl phosphine ligand (o-$OCH_3Ph)_3P$ (**L_3**) gave the highest yield of **3a** (78%, entry 10). Finally, different palladium sources were evaluated (entries 14–17), and $PdCl_2$ was determined to be the best, giving **3a** in 86% yield (entry 16).

Table 3. **Optimization of the Reaction Conditions for the β-Arylation of 1a**[a]



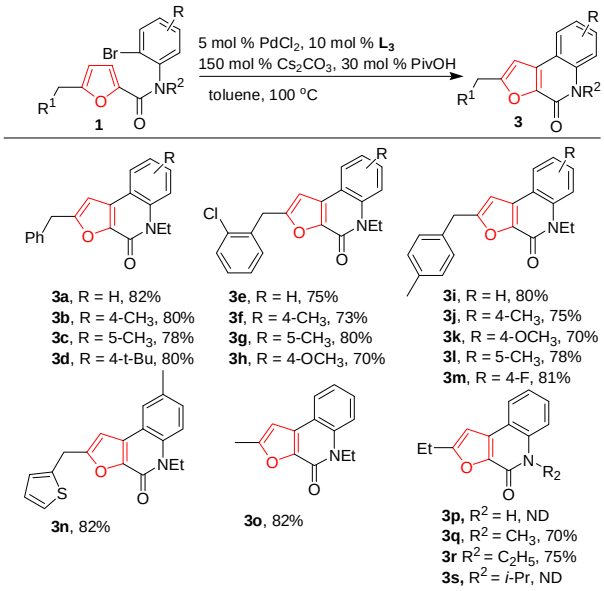
entry	[Pd]	L	solvent	yield of **3a** (%)[b]	yield of **2a** (%)[b]
1	$Pd(OAc)_2$	L_1	toluene	58	30
2[c]	$Pd(OAc)_2$	L_1	toluene	ND	85
3	$Pd(OAc)_2$	L_1	DCE	55	32
4	$Pd(OAc)_2$	L_1	CH_3CN	38	35
5	$Pd(OAc)_2$	L_1	THF	40	42
6	$Pd(OAc)_2$	L_1	1,4-dioxane	42	45
7	$Pd(OAc)_2$	L_1	DMA	45	40
8	$Pd(OAc)_2$	L_1	DMSO	30	35
9	$Pd(OAc)_2$	L_2	toluene	ND	65
10	$Pd(OAc)_2$	L_3	toluene	78	15
11	$Pd(OAc)_2$	PCy_3	toluene	60	24
12	$Pd(OAc)_2$	PPh_3	toluene	46	40
13	$Pd(OAc)_2$	Binap	toluene	50	31
14	$Pd(PPh_3)_4$	L_3	toluene	72	23
15	$Pd_2(dba)_3$	L_3	toluene	76	15
16	$PdCl_2$	L_3	toluene	86	8
17	$PdBr_2$	L_3	toluene	80	12

[a]Reaction conditions, unless otherwise noted: **1** (0.3 mmol), [Pd] (5 mol %), L (10 mol %), Cs_2CO_3 (150 mol %), PivOH (30 mol %), solvent (3 mL), under N_2, 100 °C, 12 h. **L_1** = $PCy_3{\cdot}HBF_4$, **L_2** = $(o\text{-}CH_3Ph)_3P$, **L_3** = $(o\text{-}OCH_3Ph)_3P$. ND = not detected. [b]Yields were determined by ^1H NMR analysis with mesitylene as an internal standard. [c]No PivOH was used in this reaction.

We subjected various substrates **1** with different R, R^1, and R^2 groups to the optimized conditions (Table 3, entry 16) to evaluate the generality of the β-arylation reaction (Table 4). The substrate scope was broad, and most of the substrates **1** could be transformed into 5*H*-furo[2,3-*c*]quinolin-4-ones **3** in good yields (70–82%). Specifically, R could be a H atom, an electron-donating group (Me, *t*-Bu, OMe),

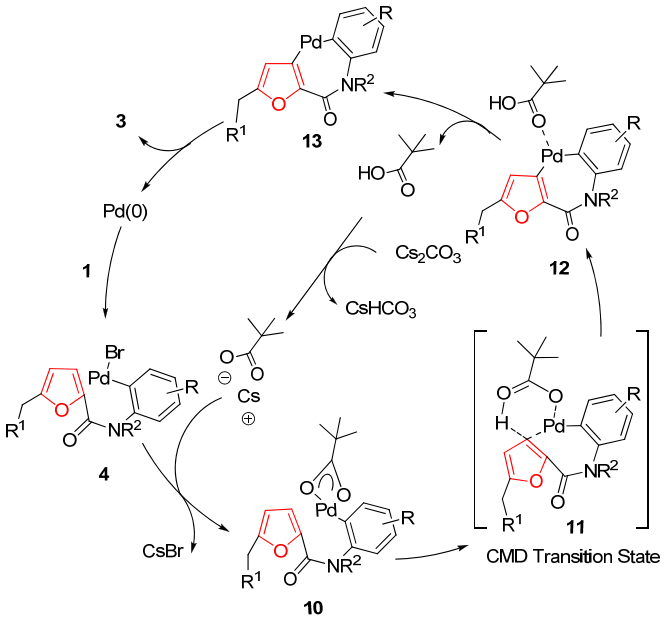
or an electron-withdrawing group (F). The R^1 substituent could be an alkyl group, a phenyl group (either unsubstituted or with an electron-donating or electron-withdrawing substituent), or a thiophenyl group. The R^2 substituent could be a small alkyl group (Me, Et), but when R^2 was H (**1p**) or a larger alkyl group (*i*-Pr, **1s**), the expected products (**3p** and **3s**, respectively) were not observed.

Table 4. Substrate Scope of the *β*-Arylation[a]



[a]Reaction conditions: **1** (0.3 mmol), toluene (3 mL), under N_2, 12 h. Yields are isolated yields.

Scheme 5. Proposed Mechanism for the Formation of 3

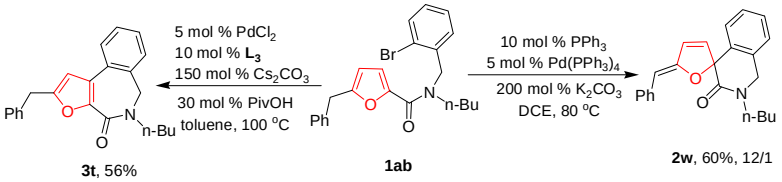


A mechanism for the formation of **3** is proposed in Scheme 5. Oxidative addition of Pd(0) to **1**

produces palladium complex **4.** Nucleophilic attack of **4** by pivalate anion produces ArPd(OPiv) complex **10**, which forms a CMD transition state (**11)** via activation of the β-C–H bond of the furan ring. After a release of PivOH, **11** is transformed into biarylpalladium species **12**, which is subsequently converted to complex **13**. Complex **13** then undergoes reductive elimination to give **3** and regenerate Pd(0).

When *N*-benzyl-2-furancarboxamide **1ab** was subjected to the optimized reaction conditions for the α- and β-arylations, the substrate was transform into [5.6]spirooxindole **2w** (60% yield, 12:1 *Z*/*E* mixture) and seven-membered lactam **3t** (56% yield), respectively (Scheme 6).

Scheme 6. Synthesis of 2w and 3t



CONCLUSION

In summary, we achieved regioselective Pd-catalyzed intramolecular direct arylation of the furan rings of *N*-(2-bromophenyl)-2-furancarboxamides using different reaction conditions to efficiently synthesize biologically interesting spirooxindoles and 5*H*-furo[2,3-*c*]quinolin-4-ones. Interestingly, when R^1 of **1** was an aryl group, *Z* and *E* favored spirooxindoles can be formed using K_2CO_3 and *t*-BuOLi as the base, respectively. We propose three possible pathways for these transformations—namely, Heck insertion, electrophilic palladation, and CMD—indicating the versatility of this Pd-catalyzed direct arylation for the transformation of furans. In particular, the dearomatizing intramolecular α-arylation that occurred without opening of the furan ring is of great significance for extending the synthetic applications of furan derivatives.

EXPERIMENTAL SECTION

General Information. IR spectra were recorded with FT-IR as a thin film or using KBr pellets and are expressed in cm^{-1}. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded using $CDCl_3$ as a solvent. Chemical shifts are reported in ppm downfield to tetramethylsilane. Coupling constants are reported and expressed in Hz; splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (double doublet), dt (double triplet), dq (double quartet), br (broad). Mass spectra were obtained from high resolution ESI mass spectrometer. All reactions were carried out using freshly distilled and dry solvents. Column chromatography was performed over silica gel (100-200 Mesh) using petroleum ether and ethyl acetate as the eluent. The structures of **S1**, **S2**, **S3**, **S4**, **S5**, **S6**, **S7** are shown in the Supporting Information.

General procedure for the preparation of 1

Method A

Synthesis of **S2**: To a solution of 5-substitued-benzoylfuran-2-carboxylate (**S1**) (10 mmol) in MeOH (20 mL) was added $NaBH_4$ (418.0 mg, 11 mmol) in portions at 0 ^{o}C. After stirring at the same temperature for 1 h, H_2O (30 mL) was added to quench the reaction. Removal of MeOH under reduced pressure provided the aqueous layer which was extracted with EtOAc (10 mL×3). The combined organic layers were washed with saturated brine, dried over Na_2SO_4, concentrated under reduced pressure, providing a colorless liquid.

To the solution of the above-made liquid in CH_2Cl_2 (40 mL) was added CF_3COOH (2.5 g, 22 mmol) then Et_3SiH (2.55 g, 22 mmol) in portions at 0 ^{o}C. The reaction was stirred for 30 minutes, then H_2O (20 mL) was added to quench the reaction. The resulting mixture was extracted with CH_2Cl_2 (10 mL×3), and the combined organic layers were washed with saturated brine, dried over sodium sulfate, concentrated under reduced pressure. The residue was purified by flash chromatography on a silica gel

(using petroleum ether/ethyl acetate = 30:1 as the eluent) to give product **S2** (**S2a-S2g**).

Methyl 5-benzylfuran-2-carboxylate (**S2a**). Colorless oil (1.85 g, 86% over 2 steps); IR (film) 2951, 1726, 1496, 1308, 1019, 797 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 2H), 7.30 – 7.27 (m, 3H), 7.12 (d, J = 3.3 Hz, 1H), 6.09 (d, J = 3.3 Hz, 1H), 4.06 (s, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 159.2, 143.4, 136.6, 128.8, 128.6, 126.9, 119.2, 108.9, 51.7, 34.7; HRMS (ESI) *m/z* calcd for $C_{13}H_{12}NaO_3$ $[M + Na]^+$: 239.0679; Found: 239.0689.

Methyl 5-(4-methylbenzyl)furan-2-carboxylate (**S2b**). Colorless oil (2.07 g, 90% over 2 steps); IR (film) 2951, 1726, 1595, 1436, 1201, 1020, 927 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 – 7.09 (m, 4H), 7.07 (d, J = 3.4 Hz, 1H), 6.04 (d, J = 3.4 Hz, 1H), 3.97 (s, 2H), 3.84 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 159.2, 143.3, 136.4, 133.6, 129.3, 128.7, 119.2, 108.7, 51.7, 34.3, 21.0; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}NaO_3$ $[M + Na]^+$: 253.0835; Found: 253.0845.

Methyl 5-(4-chlorobenzyl)furan-2-carboxylate (**S2c**). Colorless oil (2.12 g, 85% over 2 steps); IR (film) 2952, 1725, 1592, 1435, 1201, 1016, 927 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 3.4 Hz, 1H), 6.08 (d, J = 3.4 Hz, 1H), 4.00 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 158.9, 143.5, 135.1, 132.8, 130.1, 128.8, 119.3, 109.0, 51.9, 34.0; HRMS (ESI) *m/z* calcd for $C_{13}H_{11}ClNaO_3$ $[M + Na]^+$: 273.0298; Found: 273.0298.

Methyl 5-(4-methoxybenzyl)furan-2-carboxylate (**S2d**). Colorless oil (2.16 g, 88% over 2 steps); IR (film) 2951, 1725, 1604, 1437, 1249, 1027 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 3.4 Hz, 1H), 6.84 (d, J = 8.6 Hz, 2H), 6.04 (d, J = 3.4 Hz, 1H), 3.97 (s, 2H), 3.86 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 159.2, 158.5, 143.3, 129.8, 128.7, 119.2, 114.1, 108.6, 55.2, 51.7, 33.9; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}NaO_4$ $[M + Na]^+$: 269.0784; Found: 269.0793.

Ethyl 5-(2-methylbenzyl)furan-2-carboxylate (**S2e**). Colorless oil (2.09 g, using ethyl-2-furoate as the start material, 86% over 2 steps); IR (film) 2980, 1720, 1456, 1206, 965 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.17 (m, 4H), 7.09 (d, J = 3.2 Hz, 1H), 5.94 (d, J = 3.2 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 4.05 (s, 2H), 2.31 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 158.9, 143.6, 136.5, 134.9, 130.4, 129.7, 127.2, 126.2, 119.0, 108.7, 60.7, 32.6, 19.3, 14.3; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}NaO_3$ $[M + Na]^+$: 267.0992; Found: 267.1000.

Methyl 5-(thiophen-2-ylmethyl)furan-2-carboxylate (**S2f**). Colorless oil (1.89 g, 85% over 2 steps); IR (film) 2952, 1725, 1434, 1203, 1022, 927 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, J = 5.1, 1H), 7.09 (d, J = 3.4 Hz, 1H), 6.93 (dd, J = 5.1, 3.5 Hz, 1H), 6.89 (d, J = 3.4, 1H), 6.17 (d, J = 3.4 Hz, 1H), 4.22 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 158.4, 143.5, 138.4, 127.0, 126.2, 124.5, 119.2, 108.9, 51.7, 28.9; HRMS (ESI) *m/z* calcd for $C_{11}H_{10}O_3NaS$ $[M + Na]^+$: 245.0243; Found: 245.0251.

Methyl 5-(naphthalen-2-ylmethyl)furan-2-carboxylate (**S2g**). Colorless solid (2.39 g, 90% over 2 steps), mp: 68.6 – 69.5 ^oC; IR (film) 2951, 1724, 1595, 1434, 1203, 809 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.72 (m, 3H), 7.67 (s, 1H), 7.49 – 7.40 (m, 2H), 7.34 (dd, J = 8.4, 1.1 Hz, 1H), 7.09 (d, J = 3.4 Hz, 1H), 6.07 (d, J = 3.3 Hz, 1H), 4.17 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 159.2, 143.5, 134.1, 133.5, 132.4, 128.4, 127.6, 127.6, 127.4, 127.0, 126.2, 125.8, 119.3, 109.1, 51.8, 34.9; HRMS (ESI) *m/z* calcd for $C_{17}H_{14}NaO_3$ $[M + Na]^+$: 289.0835; Found: 289.0838.

Synthesis of **1**: To the solution of **S2** (5 mmol) in THF (5 mL) was added aqueous NaOH (2 N, 10 mL) slowly. The reaction was stirred at room temperature until the disappearance of **S2** according to the TLC. The organic solvent was removed under reduced pressure, then aqueous HCl (2 N) was added slowly to acidify the aqueous solution (pH = 2). The resulting mixture was extracted with EtOAc (10

mL×3), the combined organic layers were washed with saturated brine, dried over Na_2SO_4, concentrated under reduced pressure, providing a white solid (**S3**).

To a round-bottom 50 mL flask equipped with a condenser pipe and a drying tube was added the above-obtained solid (**S3**) then $SOCl_2$ (20 mL). The mixture was heated to reflux for 3 hours. The excessive $SOCl_2$ was removed under reduced pressure. Dry CH_2Cl_2 (5 mL) was added to the residue to form a clear solution. The solution was slowly added to a mixture of 2-bromoaniline (**S4**, 5.5 mmol), triethylamine (1.01 g, 10 mmol) and CH_2Cl_2 (5 mL) at 0 ^oC. After the addition, the solution was stirring at room temperature for 30 minutes, and then H_2O (30 mL) was added. The resulting mixture was extracted with EtOAc (10 mL×3), the combined organic layers were washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, The residue was purified by flash chromatography on a silica gel (using PE/ EtOAc = 12:1 as the eluent) to give product **1** (**1a-q, 1u-y, 1ab**).

5-Benzyl-N-(2-bromophenyl)-N-ethylfuran-2-carboxamide (**1a**). Colorless oil (1.21 g, 63% over 4 steps); IR (film) 2977, 2932, 1720, 1640, 1211, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 7.9, 1.2 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.29 – 7.27 (m, 2H), 7.26 – 7.24 (m, 1H), 7.24 – 7.22 (m, 1H), 7.22 – 7.18 (m, 1H), 7.07 (d, J = 7.1 Hz, 2H), 6.05 (br, 1H), 5.84 (br, 1H), 4.28 – 4.16 (m, 1H), 3.78 (s, 2H), 3.55 – 3.45 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 157.2, 146.4, 141.4, 137.0, 133.7, 131.1, 129.5, 128.7, 128.5, 128.2, 126.6, 124.2, 117.4, 108.1, 44.4, 34.4, 12.7; HRMS (ESI) *m/z* calcd for $C_{20}H_{19}BrNO_2$ $[M + H]^+$: 384.0594 ; Found: 384.0608.

5-Benzyl-N-(2-bromo-4-methylphenyl)-N-ethylfuran-2-carboxamide (**1b**). Colorless oil (1.31 g, 66% over 4 steps); IR (film) 2975, 1722, 1641, 1522, 1448, 1210, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.29 – 7.17 (m, 3H), 7.12 – 7.03 (m, 4H), 5.93 (br, 1H), 5.81 (br, 1H), 4.23 – 4.12 (m, 1H), 3.80 (s, 2H), 3.51 – 3.37 (m, 1H), 2.34 (s, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ

158.8, 157.1, 146.4, 139.9, 138.6, 137.1, 134.1, 130.7, 128.9, 128.7, 128.5, 126.6, 123.8, 117.2, 108.1, 44.4, 34.5, 20.9, 12.6; HRMS (ESI) *m/z* calcd for $C_{21}H_{21}BrNO_2$ $[M + H]^+$: 398.0750; Found: 398.0757.

5-Benzyl-N-(2-bromo-4-tert-butylphenyl)-N-ethylfuran-2-carboxamide (**1c**). Colorless oil (1.32 g, 60% over 4 steps); IR (film) 2926, 1743, 1688, 1643, 1464, 1212, 1024, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.24 – 7.13 (m, 2H), 7.08 (d, J = 7.2 Hz, 2H), 5.93 (br, 1H), 5.78 (br, 1H), 4.25 – 4.15(m, 1H), 3.76 (s, 2H), 3.52 – 3.42 (m, 1H), 1.31 (s, 9H), 1.22 (t, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 157.2, 153.4, 146.3, 138.6, 137.1, 130.7, 130.5, 128.7, 128.5, 126.6, 125.3, 123.8, 117.2, 108.1, 44.4, 34.8, 34.4, 31.2, 12.7; HRMS (ESI) *m/z* calcd for $C_{24}H_{26}BrNNaO_2$ $[M + Na]^+$: 462.1039; Found: 462.1039.

5-Benzyl-N-(2-bromo-4-methoxyphenyl)-N-ethylfuran-2-carboxamide (**1d**). Colorless oil, (1.34 g, 65% over 4 steps); IR (film) 2934, 1721, 1640, 1216, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.43 (m, 1H), 7.29 – 7.23 (m, 2H), 7.22 – 7.17 (m, 1H), 7.06 (d, J = 7.2 Hz, 2H), 6.78 – 6.72 (m, 2H), 6.09 (br, 1H), 5.85 (br, 1H), 4.21 – 4.10 (m, 1H), 3.79 (s, 2H), 3.74 (s, 3H), 3.58 – 3.45 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 158.7, 157.2, 146.3, 142.0, 137.1, 133.8, 128.7, 128.5, 126.6, 117.4, 116.6, 115.4, 114.5, 108.2, 55.7, 44.6, 34.5, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{21}BrNO_3$ $[M + H]^+$: 414.0699 ; Found: 414.0705.

5-Benzyl-N-(2-bromo-4-fluorophenyl)-N-ethylfuran-2-carboxamide (**1e**). Colorless oil (1.1 g, 55% over 4 steps); IR (film) 2930, 1719, 1639, 1451, 1264, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.21 (m, 4H), 7.18 – 7.13 (m, 1H), 7.02 (d, J = 6.7 Hz, 2H), 6.97 (t, J = 8.0 Hz, 1H), 6.28 (br, 1H), 5.91 (br, 1H), 4.22 – 4.11 (m, 1H), 3.75 (s, 2H), 3.51 – 3.40 (m, 1H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (d, $J_{C\text{-}F}$ = 253.4 Hz), 158.7, 157.2, 146.5, 137.6 (d, $J_{C\text{-}F}$ = 4.0 Hz), 136.9, 131.7 (d, $J_{C\text{-}F}$ = 9.1 Hz), 128.6, 128.5, 126.7, 124.6 (d, $J_{C\text{-}F}$ = 10.2 Hz), 120.7 (d, $J_{C\text{-}F}$ = 25.2 Hz), 117.8, 115.2

(d, $J_{C\text{-}F}$ = 22.2 Hz), 108.3, 44.5, 34.5, 12.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}BrFNO_2$ $[M + H]^+$: 402.0499; Found: 402.0511.

N-(2-Bromophenyl)-N-ethyl-5-(4-methylbenzyl)furan-2-carboxamide (**1f**). Colorless oil (1.23 g, 62% over 4 steps); IR (film) 2976, 1641, 1480, 1211, 1023, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 7.9, 1.3 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.26 – 7.18 (m, 2H), 7.08 (d, J = 7.9 Hz, 2H), 6.97 (d, J = 7.8 Hz, 2H), 6.03 (d, J = 2.2 Hz, 1H), 5.82 (d, J = 2.2 Hz, 1H), 4.26 – 4.18 (m, 1H), 3.74 (s, 2H), 3.56 – 3.47 (m, 1H), 2.33 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 157.6, 146.3, 141.4, 136.1, 133.9, 133.7, 131.1, 129.4, 129.1, 128.6, 128.2, 124.2, 117.4, 107.9, 44.4, 34.0, 21.0, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{21}BrNO_2$ $[M + H]^+$: 398.0750 ; Found: 398.0762.

N-(2-Bromo-4-methylphenyl)-N-ethyl-5-(4-methylbenzyl)furan-2-carboxamide (**1g**). Colorless oil (1.33 g, 65% over 4 steps); IR (film) 2975, 1642, 1446, 1210, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.10 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 7.8 Hz, 2H), 6.96 (d, J = 7.8 Hz, 2H), 5.91 (br, 1H), 5.78 (br, 1H), 4.25 – 4.12 (m, 1H), 3.76 (s, 2H), 3.50 – 3.41 (m, 1H), 2.35 (s, 3H), 2.31 (s, 3H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 157.5, 146.2, 139.9, 138.7, 136.1, 134.1, 134.0, 130.7, 129.1, 128.9, 128.6, 123.8, 117.2, 107.9, 44.4, 34.1, 21.0, 20.8, 12.6; HRMS (ESI) *m/z* calcd for $C_{22}H_{23}BrNO_2$ $[M + H]^+$: 412.0907 ; Found: 412.0920.

N-(2-Bromo-4-methoxyphenyl)-N-ethyl-5-(4-methylbenzyl)furan-2-carboxamide (**1h**). Colorless oil (1.45 g, 68% over 4 steps); IR (film) 2931, 1642, 1473, 1216, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 9.6 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H), 6.98 (d, J = 7.8 Hz, 2H), 6.84 – 6.76 (m, 2H), 6.10 (br, 1H), 5.85 (br, 1H), 4.21 – 4.12 (m, 1H), 3.77 (s, 2H), 3.77 (s, 3H), 3.58 – 3.49 (m, 1H), 2.33 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 158.7, 157.6, 146.2, 142.1, 136.1, 134.0, 133.8, 129.2, 128.6, 117.4, 116.6, 115.4, 114.5, 107.9, 55.7, 44.6, 34.1, 21.0, 12.7; HRMS (ESI) *m/z*

calcd for $C_{22}H_{23}BrNO_3$ $[M + H]^+$: 428.0856 ; Found: 428.0869.

N-(2-Bromo-5-methylphenyl)-N-ethyl-5-(4-methylbenzyl)furan-2-carboxamide (**1i**). Colorless oil (1.34 g, 65% over 4 steps); IR (film) 2976, 1643, 1472, 1211, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.1 Hz, 1H), 7.08 – 7.02 (m, 3H), 7.00 (d, J = 8.2 Hz, 1H), 6.95 (d, J = 7.8 Hz, 2H), 5.97 (br, 1H), 5.80 (br, 1H), 4.20 – 4.10 (m, 1H), 3.74 (s, 2H), 3.54 – 3.44 (m, 1H), 2.30 (s, 3H), 2.28 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 157.5, 146.3, 141.1, 138.5, 136.1, 134.0, 133.2, 131.6, 130.3, 129.1, 128.6, 120.6, 117.3, 107.9, 44.5, 34.1, 21.0, 20.8, 12.7; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}BrNNaO_2$ $[M + Na]^+$: 434.0726; Found: 434.0728.

N-(2-Bromophenyl)-5-(4-chlorobenzyl)-N-ethylfuran-2-carboxamide (**1j**). Colorless oil (1.25 g, 60% over 4 steps); IR (film) 2976, 1743, 1641, 1482, 1210, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.9 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.25 – 7.14 (m, 4H), 6.97 (d, J = 8.0 Hz, 2H), 6.05 (br, 1H), 5.84 (br, 1H), 4.28 – 4.09 (m, 1H), 3.73 (s, 2H), 3.55– 3.42 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 156.4, 146.6, 141.3, 135.5, 133.7, 132.5, 131.1, 130.0, 129.5, 128.6, 128.2, 124.1, 117.3, 108.3, 44.5, 33.8, 12.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}BrClNO_2$ $[M + H]^+$: 418.0204; Found: 418.0212.

N-(2-Bromo-4-methylphenyl)-5-(4-chlorobenzyl)-N-ethylfuran-2-carboxamide (**1k**). Colorless oil (1.24 g, 58% over 4 steps); IR (film) 2927, 1643, 1495, 1272, 1210, 966 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.22 (d, J = 8.2 Hz, 2H), 7.08 (br, 2H), 6.99 (d, J = 8.2 Hz, 2H), 5.95 (br, 1H), 5.83 (br, 1H), 4.22 – 4.10 (m, 1H), 3.77 (s, 2H), 3.52 – 3.37 (m, 1H), 2.35 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 156.3, 146.6, 139.9, 138.6, 135.6, 134.1, 132.4, 130.6, 130.0, 128.9, 128.6, 123.7, 117.1, 108.3, 44.5, 33.8, 20.8, 12.6; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrClNO_2$ $[M + H]^+$: 432.0360; Found: 432.0373.

N-(2-Bromo-4-methylphenyl)-N-ethyl-5-(4-methoxybenzyl)furan-2-carboxamide (**1l**). Colorless oil (1.32 g, 62% over 4 steps); IR (film) 2931, 1641, 1397, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.12 (br, 2H), 7.01 (d, J = 8.5 Hz, 2H), 6.81 (d, J = 8.5 Hz, 2H), 5.93 (br, 1H), 5.80 (br, 1H), 4.25 – 4.15 (m, 1H), 3.80 (s, 3H), 3.76 (s, 2H), 3.52 – 3.43 (m, 1H), 2.37 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 158.4, 157.7, 146.3, 139.9, 138.6, 134.1, 130.7, 129.7, 129.2, 128.9, 123.8, 117.2, 113.9, 107.9, 55.2, 44.4, 33.6, 20.8, 12.6; HRMS (ESI) *m/z* calcd for $C_{22}H_{23}BrNO_3$ $[M + H]^+$: 428.0856 ; Found: 428.0862.

N-(2-Bromophenyl)-N-ethyl-5-(2-methylbenzyl)furan-2-carboxamide (**1m**). Colorless oil (1.29 g, 65% over 4 steps); IR (film) 2975, 1642, 1474, 1211, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.9 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.26 – 7.20 (m, 2H), 7.15 – 7.11 (m, 3H), 6.98 (d, J = 6.6 Hz, 1H), 5.98 (br, 1H), 5.71 (br, 1H), 4.27 – 4.17 (m, 1H), 3.78 (s, 2H), 3.58 – 3.48 (m, 1H), 2.19 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 156.9, 146.2, 141.4, 136.4, 135.2, 133.7, 131.1, 130.3, 129.7, 129.5, 128.2, 126.9, 126.1, 124.2, 117.4, 108.1, 44.4, 32.2, 19.4, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{21}BrNO_2$ $[M + H]^+$: 398.0750; Found: 398.0757.

N-(2-Bromophenyl)-5-(2-chlorobenzyl)-N-ethylfuran-2-carboxamide (**1n**). Colorless oil (1.27 g, 61% over 4 steps); IR (film) 2929, 1701, 1472, 1270, 1025, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, J = 7.9, 1.0 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.25 – 7.15 (m, 4H), 7.04 – 7.01 (m, 1H), 6.08 (br, 1H), 5.87 (br, 1H), 4.26 – 4.16 (m, 1H), 3.90 (s, 2H), 3.56 – 3.46 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 155.4, 146.5, 141.4, 134.9, 133.9, 133.7, 131.1, 130.8, 129.4, 128.2, 128.1, 126.9, 126.9, 124.1, 117.4, 108.7, 44.4, 31.9, 12.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}BrClNNaO_2$ $[M + Na]^+$: 440.0023; Found: 440.0024.

N-(2-Bromo-4-methylphenyl)-N-ethyl-5-(thiophen-2-ylmethyl)furan-2-carboxamide (**1o**). Colorless oil

(1.1 g, 55% over 4 steps); IR (film) 2927, 1743, 1642, 1391, 1271, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.16 (dd, J = 5.1, 0.7 Hz, 1H), 7.13 (s, 2H), 6.94 – 6.91 (m, 1H), 6.76 (s, 1H), 5.92 (br, 2H), 4.29 – 4.11 (m, 1H), 4.03 (s, 2H), 3.54 – 3.45 (m, 1H), 2.38 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 156.0, 146.4, 140.0, 138.9, 138.6, 134.1, 130.7, 129.1, 126.8, 125.9, 124.2, 123.7, 117.1, 108.1, 44.4, 28.7, 20.9, 12.6; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}BrNNaO_2S$ $[M + Na]^+$: 426.0134; Found: 426.0146.

N-(2-Bromophenyl)-N-ethyl-5-(naphthalen-2-ylmethyl)furan-2-carboxamide (**1p**). Colorless oil (1.15 g, 53% over 4 steps); IR (film) 2975, 1744, 1688, 1473, 1212, 966 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.70 (m, 3H), 7.49 –7.42(m, 4H), 7.17 (t, J = 9.1 Hz, 3H), 7.04 – 7.01 (m, 1H), 6.11 (br, 1H), 5.87 (br, 1H), 4.22 – 4.12 (m, 1H), 3.91 (s, 2H), 3.54 – 3.44 (m, 1H), 1.20 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 157.0, 146.6, 141.3, 134.5, 133.6, 133.5, 132.3, 130.9, 129.3, 128.1, 127.6, 127.6, 127.2, 127.1, 126.1, 125.6, 124.1, 117.5, 108.4, 99.9, 44.5, 34.7, 12.7; HRMS (ESI) *m/z* calcd for $C_{24}H_{21}BrNO_2$ $[M + H]^+$: 434.0750; Found: 434.0761.

N-(2-Bromo-4-methylphenyl)-N-ethyl-5-(naphthalen-2-ylmethyl)furan-2-carboxamide (**1q**). Colorless oil (1.20 g, 54% over 4 steps); IR (film) 2974, 1641, 1448, 1211, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.69 (m, 3H), 7.54 – 7.40 (m, 3H), 7.32 (s, 1H), 7.19 (d, J = 8.3 Hz, 1H), 7.07 (d, J = 7.9 Hz, 1H), 7.02 (d, J = 8.0 Hz, 1H), 5.99 (br, 1H), 5.86 (br, 1H), 4.22 – 4.12 (m, 1H), 3.97 (s, 2H), 3.49 – 3.40 (m, 1H), 2.22 (s, 3H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 146.5, 139.9, 138.6, 134.6, 134.0, 133.5, 132.3, 130.6, 128.9, 128.1, 127.6, 127.6 127.1, 127.1, 126.1, 125.6, 123.7, 117.2, 108.4, 99.9, 44.4, 34.6, 20.7, 12.6; HRMS (ESI) *m/z* calcd for $C_{25}H_{23}BrNO_2$ $[M + H]^+$: 448.0907; Found: 448.0914.

5-Benzyl-N-(2-bromo-5-methylphenyl)-N-ethylfuran-2-carboxamide (**1u**). Colorless oil (1.24 g, 62%

over 4 steps); IR (film) 2964, 1642, 1452, 1269, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.1 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.24 – 7.19 (m, 1H), 7.08 (d, J = 7.1 Hz, 2H), 7.06 (s, 1H), 7.02 (d, J = 8.2 Hz, 1H), 6.01 (br, 1H), 5.84 (br, 1H), 4.22 – 4.12 (m, 1H), 3.81 (s, 2H), 3.57 – 3.47 (m, 1H), 2.30 (s, 3H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 157.1, 146.3, 139.9, 138.6, 137.1, 134.1, 130.7, 128.9, 128.7, 128.4, 126.5, 123.7, 117.2, 108.1, 44.4, 34.5, 20.8, 12.6; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}BrNNaO_2$ $[M + Na]^+$: 420.0570; Found: 420.0572.

N-(2-Bromo-4-methylphenyl)-5-(2-chlorobenzyl)-N-ethylfuran-2-carboxamide(**1v**). Colorless oil (1.29 g, 60% over 4 steps); IR (film) 2928, 1700, 1643, 1390, 1210, 824 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (s, 1H), 7.36 – 7.30 (m, 1H), 7.19 – 7.14 (m, 2H), 7.10 (s, 2H), 7.04 – 7.01 (m, 1H), 6.00 (br, 1H), 5.86 (br, 1H), 4.23 – 4.13 (m, 1H), 3.93 (s, 2H), 3.52 – 3.42 (m, 1H), 2.35 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 155.3, 146.5, 139.9, 138.6, 134.9, 134.1, 133.8, 130.7, 130.6, 129.4, 128.9, 128.1, 126.9, 123.7, 117.2, 108.7, 44.4, 32.0, 20.8, 12.6; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}BrClNNaO_2$ $[M + Na]^+$: 454.0180; Found: 454.0181.

N-(2-Bromo-5-methylphenyl)-5-(2-chlorobenzyl)-N-ethylfuran-2-carboxamide (**1w**). Colorless oil (1.39 g, 66% over 4 steps); IR (film) 2967, 1701, 1642, 1472, 1211, 968 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.1 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.21 – 7.13 (m, 2H), 7.08 – 6.96 (m, 3H), 6.05 (br, 1H), 5.87 (br, 1H), 4.21 – 4.11 (m, 1H), 3.92 (s, 2H), 3.57 – 3.47 (m, 1H), 2.29 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 155.3, 146.5, 141.0, 138.5, 134.9, 133.9, 133.2, 131.5, 130.7, 130.3, 129.4, 128.1, 126.9, 120.6, 117.3, 108.7, 44.5, 32.0, 20.8, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}BrClNNaO_2$ $[M + Na]^+$: 454.0180; Found: 454.0183.

N-(2-Bromo-4-methoxyphenyl)-5-(2-chlorobenzyl)-N-ethylfuran-2-carboxamide (**1x**). Colorless oil (1.36 g, 61% over 4 steps); IR (film) 2931, 1700, 1391, 1219, 969 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ

7.37 – 7.29 (m, 1H), 7.21 – 7.15 (m, 2H), 7.14 – 7.09 (m, 2H), 7.05 – 7.01 (m, 1H), 6.83 (dd, J = 8.7, 1.9 Hz, 1H), 5.99 (br, 1H), 5.87 (br, 1H), 4.25 – 4.11 (m, 1H), 3.95 (s, 2H), 3.81 (d, J = 2.3 Hz, 3H), 3.49 –3.36 (m, 1H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 158.9, 155.4, 146.5, 134.9, 133.9, 133.8, 131.4, 130.7, 129.4, 128.1, 126.9, 124.6, 118.6, 117.2, 113.9, 108.7, 55.7, 44.4, 32.0, 12.6; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}BrClNNaO_3$ $[M + Na]^+$: 470.0129; Found: 470.0129.

N-(2-Bromo-4-fluorophenyl)-N-ethyl-5-(4-methylbenzyl)furan-2-carboxamide (**1y**). Colorless oil (1.03 g, 50% over 4 steps); IR (film) 2976, 1744, 1643, 1425, 1182, 976 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (dd, J = 8.8, 5.7 Hz, 1H), 7.06 (d, J = 7.9 Hz, 2H), 6.96 (dd, J = 8.7, 2.9 Hz, 1H), 6.94 – 6.89 (m, 3H), 6.36 (d, J = 3.1 Hz, 1H), 5.89 (d, J = 3.1 Hz, 1H), 4.18 – 4.08 (m, 1H), 3.69 (s, 2H), 3.55 – 3.45 (m, 1H), 2.31 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (d, $J_{C\text{-}F}$ = 250.6 Hz), 158.5, 157.6, 146.3, 142.7 (d, $J_{C\text{-}F}$ = 9.9 Hz), 136.2, 134.1 (d, $J_{C\text{-}F}$ = 8.9 Hz), 133.9, 129.2, 128.5, 118.7, 118.3 (d, $J_{C\text{-}F}$ = 22.7 Hz), 117.9, 116.6 (d, $J_{C\text{-}F}$ = 22.1 Hz), 108.1, 44.6, 34.1, 21.0, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}BrFNO_2$ $[M + Na]^+$: 438.0475; Found: 438.0472.

5-Benzyl-N-(2-bromobenzyl)-N-butylfuran-2-carboxamide (**1ab**). Colorless oil (1.06 g, 50% over 4 steps); IR (film) 2926, 1684, 1626, 1425, 1202, 965 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.1 Hz, 1H), 7.28 – 6.81 (m, 9H), 6.04 (br, 1H), 4.81 (s, 2H), 4.09 – 3.68 (m, 2H), 3.45 (s, 2H), 1.69 – 1.57 (m, 2H), 1.39 – 1.11 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 156.8, 147.0, 137.0, 136.8, 136.7, 132.7, 128.7, 128.6, 128.4, 127.7, 126.7, 122.4, 118.0, 108.2, 47.7, 47.6, 34.7, 29.6, 20.1, 13.9; HRMS (ESI) *m/z* calcd for $C_{23}H_{24}BrNNaO_2$ $[M + Na]^+$: 448.0883; Found: 448.0882.

Method B

To a solution of 2-substitued furan **S5** (6 mmol) in anhydrous THF (6 mL), at -10 ^{o}C under nitrogen

atmosphere, was added a solution of *n*-BuLi (2.1 mL, 1.6 M in hexane, 3.3 mmol). The solution was stirred for 1 h at the same temperature and then a solution of **S6** (3 mmol) in anhydrous THF (2 mL) was added. The reaction mixture was stirred for 30 minutes, then was quenched with saturated aq. NH_4Cl (4 mL). The organic solvent was evaporated under reduced pressure and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with saturated brine, dried over sodium sulfate, concentrated under reduced pressure to provide the crude product (**S7**) which was submitted to the next step without further purification.

The mixture of above-made crude product **S7**, R_2I (10 mmol), K_2CO_3 (1.2g, 9 mmol) and CH_3CN (5 mL) was stirred at 80 ^oC under nitrogen atmosphere for 8 h. The reaction mixture was filtered and concentrated. The residue was purified by flash chromatography on a silica gel (using petroleum ether/ethyl acetate = 12:1 as the eluent) to give product **1** (**1r-t**, **1z**, and **1aa**).

N-(2-Bromo-4-(trifluoromethyl)phenyl)-N-ethyl-5-methylfuran-2-carboxamide (**1r**). Colorless oil (0.63 g, 56% over 2 steps); IR (film) 2934, 1744, 1647, 1425, 1216, 960 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1H), 7.54 (s, 1H), 7.51 (d, J = 8.2 Hz, 1H), 6.19 (br, 1H), 5.87 (br, 1H), 4.25 – 4.16 (m, 1H), 3.60 – 3.51 (m, 1H), 2.08 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 155.1, 145.6, 142.4, 134.3, 130.9 (d, $J_{C\text{-}F}$ = 33.6 Hz), 128.6, 128.1 (q, $J_{C\text{-}F}$ = 4.0 Hz), 125.8 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.2 (q, $J_{C\text{-}F}$ = 273.4 Hz), 118.1, 107.7, 44.5, 13.4, 12.8; HRMS (ESI) *m/z* calcd for $C_{15}H_{14}BrF_3NO_2$ $[M + H]^+$: 376.0155; Found: 376.0164.

N-(2-Bromophenyl)-5-ethyl-N-methylfuran-2-carboxamide (**1s**). Colorless oil (0.54 g, 58% over 2 steps); IR (film) 2974, 1644, 1424, 1215, 946 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.64 (m, 1H), 7.41 – 7.32 (m, 1H), 7.31 – 7.22 (m, 2H), 6.03 (br, 1H), 5.84 (br, 1H), 3.34 (s, 3H), 2.46 (q, J = 7.3 Hz, 2H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 159.3, 145.5, 143.3, 133.7, 130.1,

129.6, 128.7, 123.5, 117.4, 106.1, 36.9, 21.3, 11.6; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}BrNNaO_2$ [M + Na]$^+$: 330.0100; Found: 330.0099

N-(2-Bromophenyl)-N,5-diethylfuran-2-carboxamide (**1t**). Colorless oil (0.58 g, 60% over 2 steps); IR (film) 2976, 1642, 1471, 1211, 949 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.61 (m, 1H), 7.38 – 7.31 (m, 1H), 7.27 – 7.21 (m, 2H), 5.97 (br, 1H), 5.83 (br, 1H), 4.26 – 4.16 (m, 1H), 3.54 – 3.44 (m, 1H), 2.46 (q, J = 7.2 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 158.8, 145.7, 141.6, 133.7, 131.2, 129.5, 128.3, 124.3, 117.3, 106.0, 44.4, 21.3, 12.7, 11.6; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}BrNNaO_2$ [M + Na]$^+$: 344.0257; Found: 344.0255.

N-(2-Bromophenyl)-N-ethyl-5-methylfuran-2-carboxamide (**1z**). Colorless oil (0.46 g, 50% over 2 steps); IR (film) 2975, 1701, 1642, 1445, 1215, 961 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.0 Hz, 1H), 7.41 – 7.34 (m, 1H), 7.31 – 7.24 (m, 2H), 5.80 (br, 1H), 5.68 (br, 1H), 4.27 – 4.17 (m, 1H), 3.55 – 3.47 (m, 1H), 2.17 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 154.9, 145.5, 141.4, 133.8, 131.3, 129.6, 128.4, 124.3, 117.1, 107.6, 44.3, 13.6, 12.7; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}BrNNaO_2$ [M + Na]$^+$: 330.0100; Found: 330.0099.

N-(2-Bromophenyl)-5-ethyl-N-isopropylfuran-2-carboxamide (**1aa**). Colorless oil (0.42 g, 42% over 2 steps); IR (film) 2976, 1642, 1471, 1211, 949 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.9 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.32 (d, J = 7.8 Hz, 1H), 7.30 – 7.23 (m, 1H), 5.86 (br, 1H), 5.81 (br, 1H), 4.98 – 4.85 (m, 1H), 2.47 (q, J = 7.3 Hz, 2H), 1.38 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 6.8 Hz, 3H), 1.04 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 158.8, 146.1, 139.5, 133.7, 131.6, 129.5, 127.9, 126.3, 116.9, 105.9, 49.6, 21.9, 21.3, 19.1, 11.6; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}BrNNaO_2$ [M + Na]$^+$: 358.0413; Found: 358.0418.

General procedure for the preparation of 2 (*Z*-isomer as the major)

To the mixture of K_2CO_3 (83 mg, 0.6 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol, 5 mol %), and PPh_3 (8 mg, 0.03 mmol, 10 mol %) in a Schlenk flask was added a solution of **1** (0.3 mmol) in DCE (3 mL) under nitrogen atmosphere. The reaction was stirred at 80 °C for 12 h. H_2O (5 mL) was added to the reaction and the resulting mixture was extracted with ethyl acetate (3× 5 mL). The combined organic extracts were washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography on a silica gel (using petroleum ether/ethyl acetate = 15:1 as the eluent) to give product **2** (*Z*-isomer as the major).

(Z)-5-Benzylidene-1'-ethyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2a**). Colorless oil (82.7 mg, 91%, *Z/E* = 12/1); IR (film) 2925, 1730, 1650, 1368, 1214, 1023 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 7.4 Hz, 2H), 7.45 – 7.38 (m, 1H), 7.29 – 7.24 (m, 3H), 7.14 – 7.07 (m, 2H), 6.95 (d, J = 7.9 Hz, 1H), 6.66 (d, J = 5.7 Hz, 1H), 6.08 (d, J = 5.7 Hz, 1H), 5.60 (s, 1H), 3.93 – 3.71 (m, 2H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 158.9, 142.9, 135.9, 130.9, 130.8, 130.5, 128.3, 128.2, 126.5, 125.7, 125.4, 123.2, 108.9, 101.1, 92.8, 35.3, 12.7; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}NO_2$ $[M + H]^+$: 304.1332; Found: 304.1339.

(Z)-5-Benzylidene-1'-ethyl-5'-methyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2b**). Yellow solid (76 mg, 80%, *Z/E* = 13/1), mp: 157.1 – 157.6 °C; IR (film) 2979, 2930, 1726, 1653, 1449, 1218, 1006 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.5 Hz, 2H), 7.26 – 7.20 (m, 2H), 7.18 – 7.14 (m, 1H), 7.11 – 7.06 (m, 1H), 7.04 (s, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.61 (d, J = 5.6 Hz, 1H), 6.04 (d, J = 5.6 Hz, 1H), 5.55 (s, 1H), 3.85 – 3.69 (m, 2H), 2.29 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 159.1, 140.4, 135.9, 132.9, 131.1, 131.0, 130.4, 128.3, 128.2, 126.5, 126.2, 125.7, 108.6, 101.0, 93.0, 35.3, 20.9, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_2$ $[M + H]^+$: 318.1489; Found: 318.1500.

(Z)-5-Benzylidene-5'-tert-butyl-1'-ethyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2c**). Colorless oil (88.3

mg, 82%, *Z/E* = 12/1); IR (film) 2979, 1724, 1610, 1449, 1217, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.12 – 7.06 (m, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.63 (d, *J* = 5.6 Hz, 1H), 6.05 (d, *J* = 5.6 Hz, 1H), 5.57 (s, 1H), 3.83 – 3.73 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 159.1, 146.6, 140.5, 135.9, 131.1, 130.5, 128.2, 128.1, 127.5, 126.2, 125.6, 122.5, 108.4, 100.9, 93.1, 35.2, 34.6, 31.5, 12.7; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_2$ $[M + Na]^+$: 382.1777; Found: 382.1786.

(Z)-5-Benzylidene-1'-ethyl-5'-methoxy-5H-spiro[furan-2,3'-indolin]-2'-one (**2d**). Colorless oil (74.9 mg, 75%, *Z/E* = 10/1); IR (film) 2977, 1728, 1458, 1218, 967 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 2H), 7.25 – 7.19 (m, 2H), 7.13 (d, *J* = 8.2 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.60 (d, *J* = 5.6 Hz, 1H), 6.57 – 6.51 (m, 1H), 6.48 (s, 1H), 6.01 (d, *J* = 5.6, 1H), 5.53 (s, 1H), 3.84 (s, 3H), 3.81 – 3.70 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 172.6, 162.3, 158.9, 144.4, 135.9, 130.9, 130.4, 128.2, 128.2, 126.4, 125.6, 118.3, 106.6, 100.9, 97.1, 92.7, 55.7, 35.3, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_3$ $[M + H]^+$: 334.1438; Found: 334.1450.

(Z)-5-Benzylidene-1'-ethyl-5'-fluoro-5H-spiro[furan-2,3'-indolin]-2'-one (**2e**). Colorless oil (87.6 mg, 91%, *Z/E* = 12/1); IR (film) 2981, 1728, 1654, 1455, 1213, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.61 (d, *J* = 7.8 Hz, 2H), 7.32 – 7.25 (m, 2H), 7.17 – 7.06 (m, 2H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.86 (dd, *J* = 8.3, 3.1 Hz, 1H), 6.68 (d, *J* = 5.5 Hz, 1H), 6.07 (d, *J* = 5.5 Hz, 1H), 5.62 (s, 1H), 3.90 – 3.66 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 171.9, 159.1 (d, $J_{C\text{-}F}$ = 243.4 Hz), 158.7, 138.7, 135.6, 130.9, 130.3, 128.3, 128.2, 128.1 (d, $J_{C\text{-}F}$ = 7.6 Hz), 125.9, 117.2 (d, $J_{C\text{-}F}$ = 23.7 Hz), 113.4 (d, $J_{C\text{-}F}$ = 24.9 Hz), 109.5 (d, $J_{C\text{-}F}$ = 7.7 Hz), 101.6, 92.6, 35.4, 12.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}FNO_2$ $[M + H]^+$: 322.1238; Found: 322.1249.

(Z)-1'-Ethyl-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2f**). Colorless oil (77.9 mg,

82%, *Z/E* = 10/1); IR (film) 2927, 1725, 1655, 1475, 1214, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.4 Hz, 2H), 7.41 –7.32 (m, 1H), 7.22 (d, *J* = 7.3 Hz, 1H), 7.08 – 7.01 (m, 3H), 6.91 (d, *J* = 7.8 Hz, 1H), 6.63 (d, *J* = 5.7 Hz, 1H), 6.00 (d, *J* = 5.7 Hz, 1H), 5.53 (s, 1H), 3.89 – 3.65 (m, 2H), 2.28 (s, 3H), 1.33 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 158.4, 142.9, 135.4, 132.9, 130.8, 130.5, 130.3, 128.9, 128.2, 126.7, 125.4, 123.1, 108.8, 101.1, 92.7, 35.3, 21.2, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_2$ $[M + H]^+$: 318.1487; Found: 318.1497.

(Z)-1'-Ethyl-5'-methyl-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2g**). Colorless oil (71.5 mg, 72%, *Z/E* = 16/1); IR (film) 2979, 1724, 1655, 1449, 1217, 933 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.51 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.13 – 7.05 (m, 3H), 6.83 (d, *J* = 7.9 Hz, 1H), 6.64 (d, *J* = 5.7 Hz, 1H), 6.04 (d, *J* = 5.7 Hz, 1H), 5.57 (s, 1H), 3.91 – 3.70 (m, 2H), 2.33 (s, 3H), 2.32 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 172.1, 158.5, 140.4, 135.4, 133.0, 132.9, 130.9, 130.6, 130.4, 128.9, 128.2, 126.7, 126.2, 108.6, 100.9, 92.9, 35.3, 21.2, 20.9, 12.7; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_2$ $[M + H]^+$: 332.1645; Found: 332.1655.

(Z)-1'-Ethyl-5'-methoxy-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2h**). Colorless oil (83.3 mg, 80%, *Z/E* = 14/1); IR (film) 2934, 1728, 1618, 1459, 1218, 966 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.46 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.58 (d, *J* = 5.6 Hz, 1H), 6.53 (d, *J* = 8.2, 1H), 6.47 (s, 1H), 5.97 (d, *J* = 5.6 Hz, 1H), 5.50 (s, 1H), 3.83 (s, 3H), 3.81 – 3.70 (m, 2H), 2.28 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 172.7, 162.3, 158.3, 144.4, 135.3, 133.1, 130.5, 130.4, 128.9, 128.2, 126.4, 118.5, 106.5, 100.9, 97.1, 92.6, 55.7, 35.3, 21.2, 12.7; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_3$ $[M + H]^+$: 348.1594; Found: 348.1603.

(Z)-1'-Ethyl-6'-methyl-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2i**). Colorless oil, (69.5 mg, 70%, *Z/E* = 8/1); IR (film) 3854, 3740, 3433, 2358, 1775, 1728, 1618, 1505, 1459, 1370,

1274, 1218, 1171, 1099, 1043, 966, 832, 753, 638, 582, 518, 465 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.7 Hz, 2H), 7.09 (d, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.72 (s, 1H), 6.59 (d, *J* = 5.6 Hz, 1H), 5.98 (d, *J* = 5.6 Hz, 1H), 5.51 (s, 1H), 3.86 – 3.68 (m, 2H), 2.40 (s, 3H), 2.27 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 158.4, 143.0, 141.3, 135.3, 133.0, 130.4, 130.4, 128.8, 128.1, 125.2, 123.7, 123.6, 109.7, 100.9, 92.6, 35.2, 22.0, 21.2, 12.7; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_2$ $[M + Na]^+$: 354.1464; Found: 354.1470.

(Z)-5-(4-Chlorobenzylidene)-1'-ethyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2j**). Colorless oil (83.9 mg, 83%, *Z/E* = 14/1); IR (film) 2980, 1725, 1654, 1480, 1272, 1096, 934 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.49 (d, *J* = 8.6 Hz, 2H), 7.41 – 7.36 (m, 1H), 7.23 – 7.16 (m, 3H), 7.10 – 7.04 (m, 1H), 6.92 (d, *J* = 7.9 Hz, 1H), 6.62 (d, *J* = 5.7 Hz, 1H), 6.07 (d, *J* = 5.7 Hz, 1H), 5.51 (s, 1H), 3.86 – 3.74 (m, 2H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 171.9, 159.3, 142.9, 134.4, 131.4, 131.0, 130.9, 130.3, 129.4, 128.3, 126.3, 125.4, 123.2, 108.9, 99.9, 92.9, 35.3, 12.7; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}ClNO_2$ $[M + H]^+$: 338.0942; Found: 338.0951.

(Z)-5-(4-Chlorobenzylidene)-1'-ethyl-5'-methyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2k**). Colorless oil (84.2 mg, 80%, *Z/E* = 13/1); IR (film) 2979, 1722, 1653, 1456, 1272, 934; ^1H NMR (400 MHz, $CDCl_3$) *δ* 7.50 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.15 (m, 3H), 7.03 (s, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.61 (d, *J* = 5.7 Hz, 1H), 6.07 (d, *J* = 5.7 Hz, 1H), 5.51 (s, 1H), 3.84 – 3.69 (m, 2H), 2.30 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 171.8, 159.4, 140.4, 134.4, 133.0, 131.6, 131.2, 130.9, 130.2, 129.4, 128.3, 126.2, 126.1, 108.7, 99.9, 93.1, 35.3, 20.9, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}ClNO_2$ $[M + H]^+$: 352.1099; Found: 352.1107.

(Z)-1'-Ethyl-5-(4-methoxybenzylidene)-5'-methyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2l**). Colorless oil (83.3 mg, 80%, *Z/E* = 9/1); IR (film) 2933, 1722, 1453, 1251, 931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ*

7.55 (d, J = 8.8 Hz, 2H), 7.19 (d, J = 7.9 Hz, 1H), 7.07 (s, 1H), 6.87 – 6.75 (m, 3H), 6.63 (d, J = 5.7 Hz, 1H), 6.00 (d, J = 5.7 Hz, 1H), 5.54 (s, 1H), 3.84 – 3.74 (m, 2H), 3.79 (s, 3H), 2.32 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 157.7, 157.6, 140.4, 132.9, 130.9, 130.3, 129.9, 129.5, 128.8, 126.8, 126.2, 113.7, 108.6, 100.5, 92.8, 55.2, 35.3, 20.9, 12.7; HRMS (ESI) *m/z* calcd for $C_{22}H_{22}NO_3$ $[M + H]^+$: 348.1594; Found: 348.1606.

(Z)-1'-Ethyl-5-(2-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2m**). Colorless oil (82.7 mg, 87%, *Z/E* = 10/1); IR (film) 2931, 1724, 1473, 1214, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.7 Hz, 1H), 7.39 – 7.31 (m, 1H), 7.25 – 7.20 (m, 1H), 7.12 – 6.97 (m, 4H), 6.89 (d, J = 7.8 Hz, 1H), 6.66 (d, J = 5.6 Hz, 1H), 6.03 (d, J = 5.6 Hz, 1H), 5.66 (s, 1H), 3.82 – 3.73 (m, 2H), 2.35 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 158.9, 142.9, 134.9, 134.2, 130.8, 130.8, 130.7, 129.8, 128.7, 126.6, 125.9, 125.8, 125.4, 123.1, 108.8, 97.9, 92.6, 35.3, 20.3, 12.7; HRMS (ESI) *m/z* calcd for $C_{21}H_{20}NO_2$ $[M + H]^+$: 318.1489; Found: 318.1497.

(Z)-5-(2-Chlorobenzylidene)-1'-ethyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2n**). Colorless oil (85.9 mg, 85%, *Z/E* = 11/1); IR (film) 2980, 1777, 1654, 1480, 1215, 934 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 7.9 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.34 (d, J = 7.9 Hz, 1H), 7.25 (d, J = 7.3 Hz, 1H), 7.17 – 7.07 (m, 2H), 7.06 – 7.02 (m, 1H), 6.94 (d, J = 7.9 Hz, 1H), 6.73 (d, J = 5.5 Hz, 1H), 6.14 (d, J = 5.5 Hz, 1H), 6.03 (s, 1H), 3.91 – 3.76 (m, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 160.2, 142.9, 133.4, 131.9, 131.7, 130.9, 130.7, 129.8, 129.1, 126.6, 126.5, 126.1, 125.4, 123.2, 108.9, 96.5, 92.9, 35.3, 12.6; HRMS (ESI) *m/z* calcd for $C_{20}H_{16}ClNNaO_2$ $[M + Na]^+$: 360.0762; Found: 360.0768.

(Z)-1'-Ethyl-5'-methyl-5-(thiophen-2-ylmethylene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2o**). Colorless oil (83.3 mg, 86%, *Z/E* = 12/1); IR (film) 2978, 1726, 1461, 1218, 936 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.16 (d, J = 7.9 Hz, 1H), 7.13 – 7.07 (m, 2H), 7.03 (s, 1H), 6.96 – 6.90 (m, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.60 (d, J = 5.7 Hz, 1H), 6.05 (d, J = 5.7 Hz, 1H), 5.86 (s, 1H), 3.85 – 3.67 (m, 2H), 2.29 (s, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 157.5, 140.4, 138.9, 132.9, 131.5, 131.1, 129.1, 126.9, 126.4, 126.1, 125.2, 123.9, 108.6, 94.9, 92.9, 35.3, 20.9, 12.7; HRMS (ESI) *m/z* calcd for $C_{19}H_{18}NO_2S$ $[M + H]^+$: 324.1053; Found: 324.1062.

(Z)-1'-Ethyl-5-(naphthalen-2-ylmethylene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2p**). Colorless oil (92.4 mg, 87%, *Z/E* = 13/1); IR (film) 2934, 1728, 1653, 1471, 1270, 935 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.80 – 7.65 (m, 4H), 7.42 – 7.31 (m, 3H), 7.25 (br, 1H), 7.13 – 7.05 (m, 1H), 6.93 (d, J = 7.9 Hz, 1H), 6.68 (d, J = 5.6 Hz, 1H), 6.08 (d, J = 5.6 Hz, 1H), 5.72 (s, 1H), 3.88 – 3.76 (m, 2H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 159.4, 142.9, 133.7, 133.5, 131.9, 131.0, 130.9, 130.6, 127.9, 127.6, 127.5, 127.0, 126.6, 126.5, 125.7, 125.5, 125.2, 123.2, 108.9, 101.4, 92.9, 35.3, 12.7; HRMS (ESI) *m/z* calcd for $C_{24}H_{20}NO_2$ $[M + H]^+$: 354.1489; Found: 354.1501.

(Z)-1'-Ethyl-5'-methyl-5-(naphthalen-2-ylmethylene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2q**). Colorless solid (93.6 mg, 85%, *Z/E* = 12/1), mp: 186.5 – 187.2 °C; IR (film) 2977, 1726, 1653, 1448, 1272, 936 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.80 – 7.65 (m, 4H), 7.40 – 7.32 (m, 2H), 7.18 (d, J = 7.9 Hz, 1H), 7.07 (s, 1H), 6.82 (d, J = 8.0 Hz, 1H), 6.67 (d, J = 5.6 Hz, 1H), 6.07 (d, J = 5.6 Hz, 1H), 5.71 (s, 1H), 3.86 – 3.74 (m, 2H), 2.30 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 159.5, 140.4, 133.7, 133.6, 132.9, 131.9, 131.3, 131.1, 130.4, 127.9, 127.6, 127.5, 127.0, 126.5, 126.5, 126.2, 125.7, 125.1, 108.7, 101.2, 93.2, 35.3, 20.9, 12.7; HRMS (ESI) *m/z* calcd for $C_{25}H_{22}NO_2$ $[M + H]^+$: 368.1645; Found: 368.1654.

(Z)-1'-Ethyl-5-methylene-5'-(trifluoromethyl)-5H-spiro[furan-2,3'-indolin]-2'-one (**2r**). Colorless oil (81.4 mg, 92%); IR (film) 2985, 1729, 1626, 1452, 1213, 948 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38

– 7.29 (m, 2H), 7.07 (s, 1H), 6.59 (d, J = 5.7 Hz, 1H), 6.02 (d, J = 5.7 Hz, 1H), 4.53 (s, 1H), 4.26 (s, 1H), 3.84 – 3.71 (m, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 163.9, 143.5, 133.0 (q, $J_{C\text{-}F}$ = 32.7 Hz), 131.9, 130.2, 129.4, 125.6, 123.6 (q, $J_{C\text{-}F}$ = 273.8 Hz), 120.2 (q, $J_{C\text{-}F}$ = 4.1 Hz), 105.5 (d, $J_{C\text{-}F}$ = 3.9 Hz), 90.6, 83.9, 35.4, 12.4; HRMS (ESI) *m/z* calcd for $C_{15}H_{13}F_3NO_2$ $[M + H]^+$: 296.0893; Found: 296.0900.

(Z)-5-Ethylidene-1'-methyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2s**). Colorless oil (57.9 mg, 85%, *Z/E* = 4/1); IR (film) 2977, 1721, 1625, 1461, 1212, 966 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.14 – 7.06 (m, 1H), 6.87 (d, J = 7.8 Hz, 1H), 6.49 (d, J = 5.7 Hz, 1H), 5.88 (d, J = 5.7 Hz, 1H), 4.62 (q, J = 7.1 Hz, 1H), 3.24 (s, 3H), 1.73 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 158.7, 143.7, 130.6, 129.3, 129.0, 127.1, 125.1, 123.3, 108.6, 94.9, 90.9, 26.6, 10.7; HRMS (ESI) *m/z* calcd for $C_{14}H_{14}NO_2$ $[M + H]^+$: 228.1019; Found: 228.1015.

(Z)-1'-Ethyl-5-ethylidene-5H-spiro[furan-2,3'-indolin]-2'-one (**2t**). Colorless oil (59.3 mg, 82%, *Z/E* = 5/1); IR (film) 2977, 2935, 1721, 1611, 1461, 1212, 966 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.13 – 7.05 (m, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.48 (d, J = 5.7 Hz, 1H), 5.88 (d, J = 5.7 Hz, 1H), 4.61 (q, J = 7.1 Hz, 1H), 3.81 – 3.74 (m, 2H), 1.74 (d, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 158.7, 142.8, 135.8, 130.5, 128.9, 127.3, 125.2, 123.1, 113.6, 108.7, 94.8, 35.1, 12.5, 8.8; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}NO_2$ $[M + H]^+$: 242.1176; Found: 242.1180.

(Z)-5-Ethylidene-1'-isopropyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2u**). Colorless oil (39.1 mg, 51%, *Z/E* = 4/1); IR (film) 2975, 1707, 1609, 1468, 1210, 979 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 1H), 7.21 (d, J = 7.3 Hz, 1H), 7.06 – 6.99 (m, 2H), 6.45 (d, J = 5.7 Hz, 1H), 5.84 (d, J = 5.7 Hz, 1H), 4.61 (q, J = 7.1 Hz, 1H), 4.62 – 4.52 (m, 1H), 1.72 (d, J = 7.1 Hz, 3H), 1.51 (d, J = 2.0 Hz,

3H), 1.49 (d, J = 2.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 158.8, 142.3, 130.3, 129.5, 128.8, 127.6, 125.3, 122.6, 110.2, 94.6, 90.7, 44.3, 19.4, 19.2, 10.7; HRMS (ESI) *m/z* calcd for $C_{16}H_{17}NNaO_2$ $[M + Na]^+$: 278.1151; Found: 278.1149.

(Z)-5-Benzylidene-2'-butyl-1'H,5H-spiro[furan-2,4'-isoquinolin]-3'(2'H)-one (**2w**). Colorless oil (62.1 mg, 60%, *Z/E* = 12/1); IR (film) 2929, 1654, 1461, 1263, 941 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 7.3 Hz, 2H), 7.41 (d, J = 7.3 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.33 – 7.28 (m, 3H), 7.15 – 7.11 (m, 1H), 6.48 (d, J = 5.6 Hz, 1H), 6.26 (d, J = 5.6 Hz, 1H), 5.56 (s, 1H), 4.64 (s, 2H), 3.67 – 3.48 (m, 2H), 1.71 – 1.66 (m, 2H), 1.44 – 1.36 (m, 2H), 0.97 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 159.0, 136.2, 134.7, 132.5, 130.6, 128.5, 128.4, 128.2, 127.7, 125.8, 125.4, 125.2, 100.6, 99.9, 91.7, 49.9, 47.5, 29.3, 20.0, 13.8; HRMS (ESI) *m/z* calcd for $C_{23}H_{23}NNaO_2$ $[M + Na]^+$: 368.1621; Found: 368.1619.

General procedure for the preparation of 2 (*E*-isomer as the major)

To the mixture of *t*-BuOLi (48 mg, 0.6 mmol), $Pd(PPh_3)_4$ (17 mg, 0.015 mmol, 5 mol %), and PPh_3 (8 mg, 0.03 mmol, 10 mol %) in a Schlenk flask was added a solution of **1** (0.3 mmol) in 1,4-dioxane (3 mL) under nitrogen atmosphere. The reaction was stirred at 80 °C for 12 hours. H_2O (5 mL) was added to the reaction and the resulting mixture was extracted with EtOAc (3× 5 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography on a silica gel (using PE/EtOAc = 15:1 as the eluent) to give product **2** (*E*-isomer as the major).

(E)-5-Benzylidene-1'-ethyl-5H-spiro[furan-2,3'-indolin]-2'-one (**2a'**). Colorless oil (47.2 mg, 50%, *Z/E* = 1/2.7); IR (film) 2925, 1730, 1650, 1263, 1023 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 7.8, 1.2 Hz, 1H), 7.35 – 7.34 (m, 3H), 7.30 – 7.25 (m, 2H), 7.24 – 7.17 (m, 1H), 7.14 – 7.08 (m, 2H),

6.92 (d, J = 7.9 Hz, 1H), 6.21 (d, J = 5.8 Hz, 1H), 6.16 (s, 1H), 3.85 – 3.77 (m, 2H), 1.34 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 159.9, 142.9, 136.4, 134.3, 130.9, 128.5, 127.8, 126.3, 126.2, 125.8, 125.3, 123.2, 108.9, 101.7, 90.3, 35.2, 12.5; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}NNaO_2$ [M + Na]$^+$: 326.1151; Found: 326.1152.

(E)-1'-Ethyl-5'-methyl-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2g'**). Colorless oil (64.5 mg, 65%, *Z/E* = 1/2.1); IR (film) 2925, 1724, 1612, 1455, 1217, 933 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 7.8 Hz, 2H), 7.17 – 7.11 (m, 3H), 7.08 (d, J = 5.7 Hz, 1H), 6.91 (d, J = 7.5 Hz, 1H), 6.73 (s, 1H), 6.15 (d, J = 5.7 Hz, 1H), 6.11 (s, 1H), 3.82 – 3.72 (m, 2H), 2.42 (s, 3H), 2.36 (s, 3H), 1.33 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 159.5, 142.9, 141.3, 135.4, 133.9, 133.5, 129.2, 127.6, 126.2, 125.1, 123.6, 123.3, 109.7, 101.4, 90.1, 35.1, 22.0, 21.1, 12.6; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_2$ [M + Na]$^+$: 354.1464; Found: 354.1469.

(E)-1'-Ethyl-5'-methoxy-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2h'**). Colorless oil (52.1 mg, 50%, *Z/E* = 1/1.5); IR (film) 2928, 1722, 1648, 1461, 1278, 1033 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 7.5 Hz, 2H), 7.15 (d, J = 7.5 Hz, 2H), 7.09 (d, J = 5.7 Hz, 1H), 6.91 (d, J = 8.5 Hz, 1H), 6.86 (s, 1H), 6.82 (d, J = 8.5 Hz, 1H), 6.18 (d, J = 5.7 Hz, 1H), 6.13 (s, 1H), 3.80 (s, 3H), 3.78 – 3.72 (m, 2H), 2.37 (s, 3H), 1.33 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 159.4, 156.4, 136.0, 135.5, 133.9, 133.4, 129.2, 127.6, 127.5, 126.3, 115.8, 111.8, 109.4, 101.7, 90.4, 55.9, 35.2, 21.1, 12.5; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_3$ [M + Na]$^+$: 370.1414; Found: 370.1418.

(E)-1'-Ethyl-6'-methyl-5-(4-methylbenzylidene)-5H-spiro[furan-2,3'-indolin]-2'-one (**2i'**). Colorless oil (67.5 mg, 68%, *Z/E* = 1/2); IR (film) 2926, 1725, 1619, 1451, 1218, 1018 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 7.4 Hz, 2H), 7.21 – 7.14 (m, 3H), 7.12 – 7.07 (m, 2H), 6.80 (d, J = 7.9 Hz, 1H), 6.17 (d, J = 5.8 Hz, 1H), 6.13 (s, 1H), 3.81 – 3.74 (m, 2H), 2.37 (s, 3H), 2.34 (s, 3H), 1.32 (t, J = 7.2

Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 159.5, 140.4, 135.5, 134.0, 133.5, 132.9, 131.0, 129.2, 127.6, 126.3, 126.2, 125.9, 108.6, 101.5, 90.3, 35.2, 21.1, 20.9, 12.6; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_2$ $[M + Na]^+$: 354.1464; Found: 354.1469

General procedure for the preparation of 3

To the mixture of Cs_2CO_3 (146 mg, 0.45 mmol), PivOH (9.2 mg, 0.09 mmol), $PdCl_2$ (2.65 mg, 0.015 mmol, 5 mol %), **L_3** (10.5 mg, 0.03 mmol, 10 mol %), and toluene (3 mL) in a Schlenk flask was added a solution of **1** (0.3 mmol) in toluene (3 mL) under nitrogen atmosphere. The reaction was stirred at 80 °C until the disappearance of the starting material according to the TLC. H_2O (5 mL) was added to the reaction and the resulting mixture was extracted with ethyl acetate (3× 5 mL). The combined organic extracts were washed with brine, dried over sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography on a silica gel (using petroleum ether/ethyl acetate = 8:1 as the eluent) to give product **3**.

2-Benzyl-5-ethylfuro[2,3-c]quinolin-4(5H)-one (**3a**). Colorless oil (74.5 mg, 82%); IR (film) 2976, 1665, 1449, 1257, 956 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 7.39 – 7.33 (m, 4H), 7.32 – 7.23 (m, 2H), 6.60 (s, 1H), 4.48 (q, *J* = 7.0 Hz, 2H), 4.19 (s, 2H), 1.40 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 153.2, 141.6, 136.8, 136.5, 130.6, 129.0, 128.8, 128.6, 127.0, 124.7, 122.1, 116.9, 115.1, 102.6, 37.0, 35.0, 13.1; HRMS (ESI) *m/z* calcd for $C_{20}H_{17}NNaO_2$ $[M + Na]^+$: 326.1151; Found: 326.1153.

2-Benzyl-5-ethyl-8-methylfuro[2,3-c]quinolin-4(5H)-one (**3b**). Colorless oil (76.1 mg, 80%); IR (film) 2975, 1664, 1450, 1212, 960 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.39 – 7.32 (m, 6H), 7.30 (dd, *J* = 7.3, 4.9 Hz, 1H), 6.57 (s, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 4.19 (s, 2H), 2.44 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 153.1, 141.7, 136.5, 134.7, 131.7, 130.4, 129.8,

129.1, 128.8, 127.0, 124.6, 116.8, 114.9, 102.5, 37.0, 35.1, 20.7, 13.2; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_2$ $[M + Na]^+$: 340.1308; Found: 340.1309.

2-Benzyl-5-ethyl-7-methylfuro[2,3-c]quinolin-4(5H)-one (**3c**). Colorless oil (74.2 mg, 78%); IR (film) 2974, 1665, 1456, 1260, 959 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.9 Hz, 1H), 7.40 – 7.32 (m, 4H), 7.32 – 7.27 (m, 1H), 7.25 (s, 1H), 7.10 (d, J = 7.9 Hz, 1H), 6.57 (s, 1H), 4.47 (q, J = 7.1 Hz, 2H), 4.19 (s, 2H), 2.52 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 153.3, 141.2, 138.8, 136.9, 136.5, 130.7, 129.1, 128.8, 127.0, 124.5, 123.5, 115.3, 114.5, 102.5, 36.9, 35.0, 22.2, 13.1; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_2$ $[M + Na]^+$: 340.1308; Found: 340.1312.

2-Benzyl-8-tert-butyl-5-ethylfuro[2,3-c]quinolin-4(5H)-one (**3d**). Colorless oil (86.2 mg, 80%); IR (film) 2962, 1665, 1451, 1215, 960 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.56 (dd, J = 9.0, 2.3 Hz, 1H), 7.39 (d, J = 9.0 Hz, 1H), 7.38 – 7.31 (m, 4H), 7.31 – 7.25 (m, 1H), 6.62 (s, 1H), 4.46 (q, J = 7.1 Hz, 2H), 4.19 (s, 2H), 1.40 (t, J = 7.1 Hz, 3H), 1.37 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 153.2, 145.2, 141.7, 136.5, 134.7, 130.8, 129.1, 128.8, 127.0, 126.3, 120.8, 116.5, 114.9, 102.5, 37.0, 35.1, 34.4, 31.4, 13.2; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}NNaO_2$ $[M + Na]^+$: 382.1777; Found: 382.1782.

2-(2-Chlorobenzyl)-5-ethylfuro[2,3-c]quinolin-4(5H)-one (**3e**). Brown solid (75.8 mg, 75%), mp: 115.2 – 116.0 °C; IR (film) 2975, 1665, 1445, 1211, 955 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, J = 7.8, 1.3 Hz, 1H), 7.56 – 7.48 (m, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.38 – 7.32 (m, 1H), 7.28 – 7.23 (m, 3H), 6.60 (s, 1H), 4.47 (q, J = 7.1 Hz, 2H), 4.32 (s, 2H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 153.2, 141.7, 136.8, 134.4, 134.2, 131.2, 130.6, 129.8, 128.7, 128.6, 127.2, 124.8, 122.2, 116.9, 115.1, 103.0, 37.1, 32.7, 13.1; HRMS (ESI) *m/z* calcd for $C_{20}H_{16}ClNNaO_2$ $[M + Na]^+$: 360.0762; Found: 360.0763.

2-(2-Chlorobenzyl)-5-ethyl-8-methylfuro[2,3-c]quinolin-4(5H)-one (**3f**). Colorless solid (76.9 mg, 73%), mp: 137.4 – 137.5 °C; IR (film) 2975, 1664, 1212, 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.41 (dd, J = 5.8, 3.5 Hz, 1H), 7.36 (dd, J = 5.9, 3.4 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.27 – 7.21 (m, 2H), 6.57 (s, 1H), 4.44 (q, J = 7.1 Hz, 2H), 4.31 (s, 2H), 2.42 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 153.1, 141.8, 134.7, 134.4, 134.2, 131.8, 131.2, 130.4, 129.8, 129.7, 128.7, 127.2, 124.7, 116.7, 114.9, 102.9, 37.0, 32.8, 20.6, 13.1; HRMS (ESI) *m/z* calcd for $C_{21}H_{18}ClNNaO_2$ $[M + Na]^+$: 374.0918; Found: 374.0921.

2-(2-Chlorobenzyl)-5-ethyl-7-methylfuro[2,3-c]quinolin-4(5H)-one (**3g**). Colorless solid (84.2 mg, 80%), mp: 146.2 – 146.3 °C; IR (film) 2975, 1665, 1460, 1210, 957 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.9 Hz, 1H), 7.46 – 7.40 (m, 1H), 7.39 – 7.34 (m, 1H), 7.29 – 7.24 (m, 3H), 7.10 (d, J = 7.9 Hz, 1H), 6.58 (s, 1H), 4.47 (q, J = 7.1 Hz, 2H), 4.32 (s, 2H), 2.52 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 153.3, 141.3, 138.9, 136.9, 134.4, 134.2, 131.2, 130.6, 129.7, 128.6, 127.2, 124.6, 123.5, 115.3, 114.4, 102.9, 36.9, 32.7, 22.2, 13.1; HRMS (ESI) *m/z* calcd for $C_{21}H_{18}ClNNaO_2$ $[M + Na]^+$: 374.0918; Found: 374.0922.

2-(2-Chlorobenzyl)-5-ethyl-8-methoxyfuro[2,3-c]quinolin-4(5H)-one (**3h**). Colorless solid (77.1 mg, 70%), mp: 112.7 – 113.4 °C; IR (film) 3 2972, 1663, 1460, 1245 1, 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, J = 5.8, 3.5 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.29 – 7.25 (m, 2H), 7.24 – 7.18 (m, 1H), 7.13 (dd, J = 9.2, 2.9 Hz, 1H), 6.58 (s, 1H), 4.46 (q, J = 7.1 Hz, 2H), 4.33 (s, 2H), 3.89 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 154.8, 152.7, 142.1, 134.4, 134.2, 131.3, 131.2, 130.2, 129.8, 128.7, 127.2, 117.6, 116.9, 116.4, 107.1, 102.9, 55.7, 37.2, 32.7, 13.2; HRMS (ESI) *m/z* calcd for $C_{21}H_{18}ClNNaO_3$ $[M + Na]^+$: 390.0867; Found: 390.0867.

5-Ethyl-2-(4-methylbenzyl)furo[2,3-c]quinolin-4(5H)-one (**3i**). Colorless oil (76.1 mg, 80%); IR (film)

2975, 1665, 1455, 1209, 957 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, J = 7.8, 1.2 Hz, 1H), 7.57 – 7.49 (m, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.24 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 6.59 (s, 1H), 4.49 (q, J = 7.1 Hz, 2H), 4.16 (s, 2H), 2.37 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 153.3, 141.6, 136.8, 136.7, 133.4, 130.7, 129.5, 128.9, 128.6, 124.7, 122.1, 116.9, 115.1, 102.4, 37.0, 34.6, 21.1, 13.1; HRMS (ESI) *m/z* calcd for $C_{21}H_{19}NNaO_2$ $[M + Na]^+$: 340.1308; Found: 340.1304.

5-Ethyl-8-methyl-2-(4-methylbenzyl)furo[2,3-c]quinolin-4(5H)-one (**3j**). Colorless oil (74.5 mg, 75%); IR (film) 2974, 1665, 1449, 1213, 959 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.35 – 7.28 (m, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 6.53 (s, 1H), 4.44 (q, J = 7.1 Hz, 2H), 4.13 (s, 2H), 2.42 (s, 3H), 2.34 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.1, 141.7, 136.6, 134.7, 133.4, 131.7, 130.4, 129.7, 129.4, 128.9, 124.6, 116.8, 114.9, 102.4, 36.9, 34.7, 21.1, 20.6, 13.2; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_2$ $[M + Na]^+$: 354.1464; Found: 354.1466.

5-Ethyl-8-methoxy-2-(4-methylbenzyl)furo[2,3-c]quinolin-4(5H)-one (**3k**). Colorless oil (72.9 mg, 70%); IR (film) 2972, 1664, 1459, 1244, 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, J = 9.2 Hz, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.17 – 7.12 (m, 3H), 7.11 – 7.07 (m, 1H), 6.51 (s, 1H), 4.42 (q, J = 7.1 Hz, 2H), 4.12 (s, 2H), 3.85 (s, 3H), 2.33 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 154.8, 152.7, 141.9, 136.6, 133.4, 131.1, 130.2, 129.4, 128.9, 117.7, 116.8, 116.4, 107.0, 102.3, 55.7, 37.1, 34.6, 21.1, 13.2; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_3$ $[M + Na]^+$: 370.1414; Found: 370.1417.

5-Ethyl-7-methyl-2-(4-methylbenzyl)furo[2,3-c]quinolin-4(5H)-one (**3l**). Yellow solid (77.5 mg, 78%), mp: 90.2 – 90.3 ^oC; IR (film) 2975, 1665, 1450, 1257, 956 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.9 Hz, 1H), 7.25 – 7.18 (m, 3H), 7.15 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 7.9 Hz, 1H), 6.52 (s, 1H),

4.45 (q, J = 7.1 Hz, 2H), 4.13 (s, 2H), 2.50 (s, 3H), 2.34 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2, 153.3, 141.2, 138.8, 136.9, 136.6, 133.5, 130.7, 129.4, 128.9, 124.5, 123.4, 115.3, 114.5, 102.3, 36.9, 34.6, 22.2, 21.1, 13.1; HRMS (ESI) *m/z* calcd for $C_{22}H_{21}NNaO_2$ $[M + Na]^+$: 354.1464; Found: 354.1465.

5-Ethyl-8-fluoro-2-(4-methylbenzyl)furo[2,3-c]quinolin-4(5H)-one (**3m**). Colorless oil (81.4 mg, 81%); IR (film) 2977, 1669, 1428, 1209, 963 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.7, 6.2 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.20 – 7.11 (m, 3H), 7.04 – 6.97 (m, 1H), 6.54 (s, 1H), 4.42 (q, J = 7.1 Hz, 2H), 4.15 (s, 2H), 2.37 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (d, $J_{C\text{-}F}$ = 247.2 Hz), 162.7, 153.2, 140.8, 138.3 (d, $J_{C\text{-}F}$ = 10.6 Hz), 136.7, 133.2, 130.4, 129.5, 128.9, 126.3 (d, $J_{C\text{-}F}$ = 10.1 Hz), 113.3, 110.2 (d, $J_{C\text{-}F}$ = 23.1 Hz), 102.3, 102.0, 37.4, 34.6, 21.1, 12.9; HRMS (ESI) *m/z* calcd for $C_{21}H_{18}FNNaO_2$ $[M + Na]^+$: 358.1214; Found: 358.1212.

5-Ethyl-8-methyl-2-(thiophen-2-ylmethyl)furo[2,3-c]quinolin-4(5H)-one (**3n**). Brown solid (79.5 mg, 82%), mp: 103.1 – 103.2 ^{o}C; IR (film) 2940, 1662, 1269, 807 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.36 – 7.29 (m, 2H), 7.22 (dd, J = 5.0, 1.3 Hz, 1H), 7.03 – 6.96 (m, 2H), 6.69 (s, 1H), 4.45 (q, J = 7.1 Hz, 2H), 4.39 (s, 2H), 2.44 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 153.1, 141.8, 138.1, 134.8, 131.8, 130.3, 129.8, 127.1, 126.6, 124.7, 124.6, 116.7, 115.0, 102.6, 37.0, 29.2, 20.7, 13.1; HRMS (ESI) *m/z* calcd for $C_{19}H_{17}NNaO_2S$ $[M + Na]^+$: 346.0872; Found: 346.0872.

5-Ethyl-2-methylfuro[2,3-c]quinolin-4(5H)-one (**3o**). Colorless oil (55.8 mg, 82%); IR (film) 2976, 1716, 1665, 1449, 1211 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.8, 1.4 Hz, 1H), 7.55 – 7.50 (m, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.33 – 7.28 (m, 1H), 6.67 (s, 1H), 4.48 (q, J = 7.1 Hz, 2H), 2.54 (d, J = 0.6 Hz, 3H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 153.2, 141.4, 136.8, 130.8, 128.5, 124.7, 122.1, 116.9, 115.1, 102.0, 36.9, 14.2, 13.1; HRMS (ESI) *m/z* calcd for

$C_{14}H_{13}NNaO_2$ $[M + Na]^+$: 250.0838; Found: 250.0840.

2-Ethyl-5-methylfuro[2,3-c]quinolin-4(5H)-one (**3q**). Colorless oil (47.7 mg, 70%); IR (film) 2974, 1665, 1448, 1235, 932 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.8 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.42 (d, J = 8.5 Hz, 1H), 7.35 – 7.20 (m, 1H), 6.66 (s, 1H), 3.80 (s, 3H), 2.88 (q, J = 7.6 Hz, 2H), 1.38 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 153.7, 141.2, 137.9, 130.7, 128.5, 124.4, 122.3, 116.7, 115.2, 100.6, 29.3, 21.9, 11.9; HRMS (ESI) *m/z* calcd for $C_{14}H_{13}NNaO_2$ $[M + Na]^+$: 250.0838; Found: 250.0840.

2,5-Diethylfuro[2,3-c]quinolin-4(5H)-one (**3r**). Colorless oil (54.2 mg, 75%); IR (film) 2976, 1665, 1449, 1211, 979 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1H), 7.55 – 7.48 (m, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.28 (dd, J = 9.5, 5.3 Hz, 1H), 6.67 (s, 1H), 4.48 (q, J = 7.1 Hz, 2H), 2.88 (q, J = 7.6 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H), 1.39 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 153.3, 141.2, 136.8, 130.7, 128.5, 124.7, 122.1, 117.0, 115.1, 100.5, 36.9, 21.9, 13.1, 11.9; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}NO_2$ $[M + Na]^+$: 264.0995; Found: 264.0997.

2-Benzyl-5-butyl-5,6-dihydro-4H-benzo[e]furo[2,3-c]azepin-4-one (**3t**). Colorless oil (57.9 mg, 56%); IR (film) 2958, 1641, 1461, 1269, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 7.3 Hz, 1H), 7.43 – 7.38 (m, 1H), 7.38 – 7.32 (m, 6H), 7.31 – 7.26 (m, 1H), 6.35 (s, 1H), 4.27 (s, 2H), 4.13 (s, 2H), 3.62 (t, J = 7.4 Hz, 2H), 1.71 – 1.54 (m, 2H), 1.34 – 1.22 (m, 2H), 0.90 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 158.6, 143.7, 136.8, 135.0, 131.3, 129.5, 129.1, 128.7, 128.5, 128.3, 127.9, 126.9, 126.7, 106.3, 52.2, 47.5, 34.8, 30.7, 19.9, 13.8; HRMS (ESI) *m/z* calcd for $C_{23}H_{23}NNaO_2$ $[M + Na]^+$: 368.1621; Found: 368.1623.

Supporting Information Available: Results of NOESY experiments on **2m** and copies of ^1H, ^{13}C NMR and HRMS spectra of all the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: blyin@scut.edu.cn

Acknowledgements

This work was supported by grants from the National Natural Science Foundation of China (nos. 21272078 and 21572068) and from the Science and Technology Planning Project of Guangdong Province, China (no. 2014A020221035).

References

1. (a) Nicolaou, K. C.; Hale, C. R. H.; Nilewski, C.; Ioannidou, H. A. *Chem. Soc. Rev*., **2012**, *41*, 5185. (b) Lu, R.-J.; Tucker, J. A.; Pickens, J.; Ma, Y.-A.; Zinevitch, T.; Kirichenko, O.; Konoplev, V.; Kuznetsova, S.; Sviridov, S.; Brahmachary, E.; Khasanov, A.; Mikel, C.; Yang, Y.; Liu, C.; Wang, J.; Freel, S.; Fisher, S.; Sullivan, A.; Zhou, J.; Stanfield-Oakley, S.; Baker, B.; Sailstad, J.; Greenberg, M.; Bolognesi, D.; Bray, B.; Koszalka, B.; Jeffs, P.; Jeffries, C.; Chucholowski, A.; Sexton, C. *J. Med. Chem*. **2009**, *52*, 4481. (c) Hughes, R. A.; Moody, C. J. *Angew. Chem. Int. Ed*. **2007**, *46*, 7930..

2. (a) Kumar, N. S.; Clement, J. A.; Mohanakrishnan, A. K. *Tetrahedron*, **2009**, *65*, 822. (b) Segawa, Y.; Maekawa, T.; Itami, K. *Angew. Chem. Int. Ed*. **2015**, *54*, 66.

3. For reviews of direct arylation of five-membered heteroaromatic rings, see: (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev*. **2002**, *102*, 1359. (b) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev*., **2007**, *36*, 1173. (c) Satoh, T.; Miura, M. *Chem. Lett*. **2007**, *36*, 200. (d) Bellina, F.; Rossi, R. *Tetrahedron* **2009**, *65*, 10269. (e) Roger, J.; Gottumukkala, A. L.; Doucet, H. *ChemCatChem* **2010**, *2*, 20. (f) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew.*

Chem. Int. Ed. **2012**, *51*, 8960. (g) Rossi, R.; Bellina, F.; Lessi, M.; Manzini, C. *Adv. Synth. Catal*. **2014**, *356*, 17.

4. For selected examples, see: (a) Park, C.-H.; Ryabova, V.; Seregin, I. V.; Sromek, A. W.; Gevorgyan, V. *Org. Lett*. **2004**, *6*, 1159. (b) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc*. **2005**, *127*, 8050. (c) Martins, A.; Alberico, D.; Lautens, M. *Org. Lett*. **2006**, *8*, 4827. (d) Saha, D.; Adak, L.; Ranu, B. C. *Tetrahedron Lett.* **2010**, *51*, 5624. (e) Cao, H.; Shen, D.; Zhan, H.; Yang, L. *Synlett* **2011**, 1472. (f) Cao, H.; Lin, Y.; Zhan, H.; Du, Z.; Lin, X.; Liang, Q.-M.; Zhang, H. *RSC Advances*, **2012**, *2*, 5972.

5. (a) Glover, B.; Harvey, K.A.; Liu, B.; Sharp, M. J.; Tymoschenko, M. F. *Org. Lett*. **2003**, *5*, 301. (b) Chabert, J. F. D.; Joucla, L.; David, E.; Lemaire, M. *Tetrahedron* **2004**, *60*, 3221. (c) Colletto, C.; Islam, S.; Juliá-Hernández, F.; Larrosa, I. *J. Am. Chem. Soc*. **2016**, *138*, 1677.

6. (a) Gorelsky, S. I.; Lapointe, D.; Fagnou, K. *J. Am. Chem. Soc*. **2008**, 130, 10848; (b) Liégault, B.; Lapointe, D.; Caron, L.; Vlassova, A.; Fagnou, K. *J. Org. Chem*. **2009**, *74*, 1826.

7. (a) Gottumukkala, A. L.; Doucet, H. *Adv. Synth. Catal*. **2008**, *350*, 2183. (b) Itahara, T. *J. Org. Chem.* **1985**, *50*, 5272. (c) Joo, J. M.; Touré, B. B.; Sames, D. *J. Org. Chem.* **2010**, *75*, 4911. (d) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc*. **2005**, *127*, 8050. (e) Goikhman, R.; Jacques, T. L.; Sames, D. *J. Am. Chem. Soc*. **2009**, *131*, 3042. (f) Beck, E. M.; Grimster, N. P.; Hatley, R.; Gaunt, M. J. *J. Am. Chem. Soc*. **2006**, *128*, 2528. (g) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc*. **2008**, *130*, 8172. (h) Daniels, M. H.; Armand, J. R.; Tan, K. L. *Org. Lett*. **2016**, *18*, 3310. (i) Yanagisawa, S.; Ueda, K.; Sekizawa, H.; Itami, K. *J. Am. Chem. Soc*. **2009**, *131*, 14622. (j) Tang, D.-T. D.; Collins, K. D.; Glorius, F. *J. Am. Chem. Soc*. **2013**, *135*, 7450. (k) Ueda, K.; Amaike, K.; Maceiczyk, R. M.; Itami, K.; Yamaguchi, J. *J. Am. Chem. Soc*.

2014, *136*, 13226. (l) Maki, Y.; Goto, T.; Tsukada, N. *ChemCatChem* **2016**, *8*, 699 and ref 5c.

8. (a) Lipshutz, B. H. *Chem. Rev.* **1986**, 86, 795. (b) Bur, S. K.; Padwa, A. *Chem. Rev.* **2004**, *104*, 2401. (c) Lichtenthaler, F. W. *Acc. Chem. Res.* **2002**, *35*, 728. (d) Rosatella, A. A.; Simeonov, S. P.; Frade, R. F. M.; Afonso, C. A. M. *Green Chem.* **2011**, *13*, 754. (e) Gallezot, P. *Chem. Soc. Rev.* **2012**, *41*, 1538. (f) van Putten, R. J.; van der Waal, J. C.; de Jong, E.; Rasrendra, C. B. ; Heeres, H. J.; de Vries, J. G. *Chem. Rev.* **2013**, *113*, 1499. (g) Trushkov, I. V.; Uchuskin, M. G.; Butin, A. V. *Eur. J. Org. Chem.* **2015**, 2999.

9. For selected recent examples, see: (a) Roger, J.; Požgan, F.; Doucet, H. *Adv. Synth. Catal*. **2010**, *352*, 696. (b) Roy, D.; Mom, S.; Beaupérin, M.; Henri Doucet, H.; Hierso, J.-C. *Angew. Chem. Int. Ed*. **2010**, *49*, 6650. (c) Fu, H. Y.; Doucet, H. *Eur. J. Org. Chem*. **2011**, 7163. (d) Yan, T.; Chen, L.; Bruneau, C.; Dixneuf, P. H.; Doucet, H. *J. Org. Chem*. **2013**, *78*, 4177. (e) Juwaini, N. A. B.; Ng, J. K. P.; Seayad, J. *ACS Catal.* **2012**, *2*, 1787. (f) Li, Y.; Wang, J.; Huang, M.; Wang, Z.; Wu, Y.; Wu, Y. *J. Org. Chem*. **2014**, *79*, 2890. (g) Matsidik, R.; Martin, J.; Schmidt, S.; Obermayer, J.; Lombeck, F.; Nübling, F.; Komber, H.; Fazzi, D.; Sommer, M. *J. Org. Chem*. **2015**, *80*, 980.

10. (a) Li, P.; Chai, Z.; Zhao, G.; Zhu, S.-Z. *Tetrahedron* **2009**, *65*, 1673. (b) Ionita, M.; Roger, J.; Doucet, H. *ChemSusChem* **2010**, *3*, 367. (c) Roy, D.; Mom, S.; Roger, S.; Lucas, D.; Hierso, J.-C.; Doucet, H. *ACS Catal*. **2012**, *2*, 1033. (d) Carrër, A.; Brinet, D.; Florent, J.-C.; Rousselle, P.; Bertounesque, E. *J. Org. Chem*. **2012**, *77*, 1316.

11. (a) Larbi, K. S.; Fu, H. Y.; Laidaoui, N.; Beydoun, K.; Miloudi, A.; Abed, D. E.; Djabbar, S.; Doucet, H. *ChemCatChem* **2012**, *4*, 815. (b) Padmavathi, R.; Sankar, R.; Gopalakrishnan, B.; Parella, R.; Babu, S. A. *Eur. J. Org. Chem*. **2015**, 3727.

12. (a) Kaïm, L. EI.; Grimaud, L.; Wagschal, S. *Chem. Commun*. **2011**, *47*, 1887. (b) Yin, B.; Cai, C.;

Zeng, G.; Zhang, R.; Li, X.; Jiang, H. *Org. Lett*. **2012**, *14*, 1098. (c) Ji, F.; Yi, W.; Sun, M.; Lv, M.; Cai, C. *Mol. Diversity* **2013**, *17*, 295.

13. (a) Beccalli, E. M.; Broggini, G.; Martinelli, M.; Paladino, G.; Zoni, C. *Eur. J. Org. Chem*. **2005**, 2091. (b) Campeau, L. C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc*. **2006**, *128*, 581. (c) Ohno, H.; Iuchi, M.; Kojima, N.; Yoshimitsu, T.; Fujii, N.; Tanaka, T. *Chem. Eur. J*. **2012**, *18*, 5352. (d) Tang, F.; Chen, C.; Zhou, Y.; Lin, C.; Zhang, J. *RSC Adv*, **2014**, *4*, 51298. (e) Abe, H.; Kamimura, M.; Komatsu, Y.; Horino, Y. *Heterocycles* **2015**, *90*, 1332.

14. (a) Yin, B.-L.; Lai, J.-Q.; Zhang, Z.-R.; Jiang, H.-F. *Adv. Synth. Catal*. **2011**, *353*, 1961. (b) Yin, B.; Zeng, G.; Cai, C.; Ji, F.; Huang, L.; Li, Z.; Jiang, H. *Org. Lett*. **2012**, *14*, 616. (c) Yin, B.; Huang, L.; Wang, X.; Liu, J.; Jiang, H. *Adv. Synth. Catal*. **2013**, *355*, 370. (d) Yin, B.; Zhang, X.; Liu, J.; Li, X.; Jiang, H. *Chem. Commun*. **2014**, *50*, 8113. (e) Yin, B.; Zhang, X.; Zhang, X.; Peng, H.; Zhou, W.; Liu, B.; Jiang, H. *Chem. Commun*. **2015**, *51*, 6126. (f) Liu, J.; Zhang, X.; Peng, H.; Jiang, H.; Yin, B. *Adv. Synth. Catal*. **2015**, *357*, 727. (g) Ji, F.; Peng, H.; Zhang, X.; Lu, W.; Liu, S.; Jiang. H.; Liu, B.; Yin, B. *J. Org. Chem.* **2015**, *80*, 2092. (h) Peng, H.; Li, J.; Wang, F.; Liu, B.; Yin, B. *J. Org. Chem.* **2016**, *81*, 4939. (i) Li, J.; Peng, H.; Wang, F.; Wang, X.; Jiang, H.; Yin, B. *Org. Lett*. **2016**, *18*, 3226. (j) Zhang, X.; Liu, J.; Yang, Y.; Wang, F.; Jiang, H.; Yin, B. *Org. Chem. Front*., **2016**, *3*, 1105.

15. For reviews of the bioactivities and syntheses of spirooxindoles, see: (a) Santos, M. M. M. *Tetrahedron* **2014**, *70*, 9735. (b) Marti, C.; Carreira, E. M.; *Eur. J. Org. Chem*. **2003**, 2209. (c) Williams, R. M.; Cox, R. J. *Acc. Chem. Res*. **2003**, *36*, 127. (d) Lin, H.; Danishefsky, S. J. *Angew. Chem., Int. Ed*. **2003**, *42*, 36. (e) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed*. **2007**, *46*, 8748. (f) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003.

16. (a) Lee, Y. R.; Kim, B. S.; Kweon, H. I. *Tetrahedron* **2000**, *56*, 3867. (b) Grundon, M. F. *Nat. Prod. Rep*., **1990**, *7*, 131.

17. For a related example from our group, see: Liu, J.; Xu, X.; Li, J.; Liu, B.; Jiang, H.; Yin, B. *Chem. Commun*., **2016**, 52, 9550.

18. For a related example, see: Zhang, J.; Sha, S. C.; Bellomo, A.; Trongsiriwat, N.; Gao, F.; Tomson, N. C.; Walsh, P. J. *J. Am. Chem. Soc*. **2016**, *138*, 4260.

19. Lafrance, M.; Fagnou, K. *J. Am. Chem. Soc*. **2006**, *128*, 16496 and ref 6.