JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

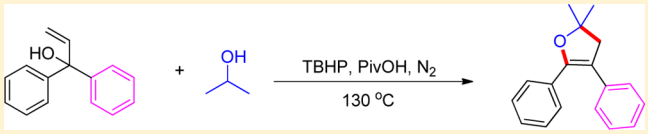
Formal [3 + 2] Reaction of α,α-Diaryl Allylic Alcohols with *sec*-Alcohols: Proceeding with Sequential Radical Addition/Migration toward 2,3-Dihydrofurans Bearing Quaternary Carbon Centers

Weiming Hu, Song Sun, and Jiang Cheng*

School of Petrochemical Engineering, Jiangsu Key Laboratory of Advanced Catalytic Materials & Technology, Jiangsu Province Key Laboratory of Fine Petrochemical Engineering, Changzhou University, Changzhou 213164, People's Republic of China

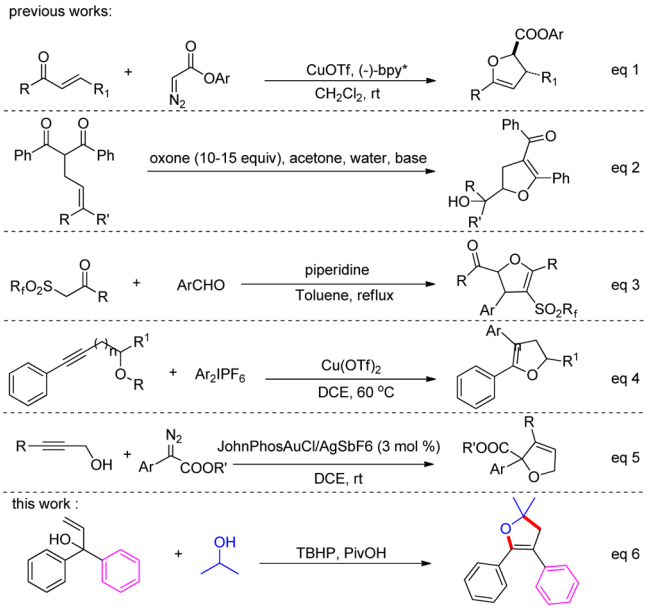
Supporting Information

ABSTRACT: An unprecedented TBHP-promoted formal [3 + 2] annulation of *sec*-alcohols with α,α-diaryl allylic alcohols has been developed, leading to 2,3-dihydrofurans in moderate to excellent yields with good functional group tolerance. This procedure involves sequential radical addition, 1,2-aryl migration, and a dehydration process, where the migration of aryl with lower electron density is favored. Notably, cyclic reactions with *sec*-alcohols also ran smoothly, providing a novel method to access oxaspiro compounds.



Dihydrofurans and their derivatives are important backbones of many bioactive natural products as well as medicinal molecules.[1,2] Besides, they serve as organic intermediates toward an array of highly functionalized tetrahydrofurans.[3] As such, a variety of synthetic approaches have been discovered (Scheme 1), including the [4 + 1] transition-metal-catalyzed cycloaddition of enones with diazo compounds (Scheme 1, eq 1),[4] ionic[5] or radical[6] reactions of olefins with 1,3-dicarbonyl compounds (Scheme 1, eq 2), as well as the formal [3 + 2] annulations of β-ketosulfides/β-ketosulfones with aldehydes (Scheme 1, eq 3).[7] Quite recently, Qu reported Cu-catalyzed intramolecular aryl etherification reactions of alkoxyl alkynes with diaryliodonium salts to construct oxo-heterocycles via cleavage of a stable C−O bond (Scheme 1, eq 4).[8] Zhang and co-workers developed a gold(I)-catalyzed formal [4 + 1] cycloaddition of α-diazoesters and propargyl alcohols toward 2,5-dihydrofurans (Scheme 1, eq 5).[9]

Scheme 1. Examples of the Synthesis of Dihydrofurans



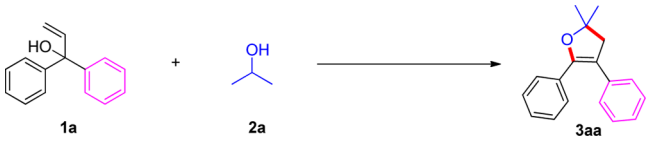
In the past, alcohol proved to be an efficient reaction partner for the construction of a C−C bond due to the activation of a sp^3 α-C−H bond by the vicinal hydroxy group.[10] Meanwhile, being nucleophilic, the hydroxyl group may take part in potentially further functionalization. Thus, with combination of the two types of reactivities, alcohol may serve as a component in the formal [*n* + 2] cyclization, leading to an oxygen-containing heterocycle. In light of the application of α,α-diaryl allylic alcohols in the construction of a variety of α-aryl-β-functionalized carbonyl ketones through radical 1,2-aryl migration,[11] we envisioned developing a novel route to construct 4,5-diaryl-2,3-dihydrofuran via such a strategy (Scheme 1, eq 6). In comparison with the reported intramolecular cyclization via C−O bond formation leading to oxygen-containing heterocycles,[12] this strategy is beneficial to the diversity and complexity of the final product, allowing one to introduce four groups into 2,3-dihydrofurans.

We commenced our study with the reaction of α,α-diphenyl allylic alcohol **1a** and isopropyl alcohol **2a** in the presence of di-*tert*-butyl peroxide (DTBP) under nitrogen atmosphere. To our delight, the reaction afforded 4,5-diaryl-2,3-dihydrofuran **3aa** in 40% yield (Table 1, entry 1). Inspired by this exciting result, we tested dicumyl peroxide (DCP), benzoyl peroxide (BPO), *tert*-butyl peroxybenzoate (TBPB), $K_2S_2O_8$, and benzoquinone (BQ). Unfortunately, they all had no positive effect on the reaction efficiency (Table 1, entries 2−6). Gratifyingly, the

Received: March 25, 2016
Published: May 2, 2016

DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405

Table 1. Optimization of the Reaction Conditions[a]



entry	oxidant[b]	acid (equiv)	yield[c] (%)
1	DTBP		40
2	DCP		32
3	BPO		8
4	TBPB		12
5	$K_2S_2O_8$		<1
6	BQ		<1
7	TBHP		56
8	TBHP	PivOH (2.0)	60
9	TBHP	CH_3COOH (2.0)	42
10	TBHP	hexanoic acid (2.0)	50
11		PivOH (2.0)	<1
12	TBHP	PivOH (0.05)	69
13	TBHP	PivOH (0.1)	84, 45,[d] 69,[e] 70,[f] 78,[g] 75[h]
14	TBHP	PivOH (1.0)	65
15	TBHP	PivOH (2.5)	58
16	TBHP	PivOH (0.1)	49,[i] 67,[j] 81[k]

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (2 mL), oxidant (4.0 equiv) at 130 °C under N_2 for 24 h in a sealed tube. [b]DTBP = di-*tert*-butyl peroxide, DCP = dicumyl peroxide, BPO = benzoyl peroxide, TBPB = *tert*-butyl peroxybenzoate, BQ = 1,4-benzoquinone, TBHP = *tert*-butyl hydroperoxide (70% in water). [c]Isolated yields. [d]Under O_2. [e]Under air. [f]At 110 °C. [g]At 120 °C. [h]At 140 °C. [i]**2a** (1.0 mL). [j]**2a** (1.5 mL). [k]**2a** (2.5 mL).

yield increased to 56% when *tert*-butyl hydroperoxide (TBHP) was used (Table 1, entry 7). Considering that a proton might take part in the dehydration process, pivalic acid, acetic acid, and *n*-hexylic acid were tested. They all had some effect on the reaction efficiency (Table 1, entries 8−10), among which the pivalic acid was the best (**3aa**, 60%). Blank experiment revealed that no reaction took place without DTBP (Table 1, entry 11). Further screening of the parameters, such as the loading of pivalic acid, the amount of solvent, reaction atmosphere, and temperature, established the optimized condition as follows: α,α-diphenyl allylic alcohol **1a** (0.2 mmol, 1 equiv), TBHP (4 equiv), and pivalic acid (0.1 equiv) in isopropyl alcohol **2a** (2 mL) at 130 °C for 24 h under N_2 (Table 1, entries 12−16), where the yield of **3aa** reached 84% (Table 1, entry 13).

With the optimal conditions in hand (Table 1, entry 13), we next evaluated the substrate scope of this procedure. Initially, various α,α-diaryl allylic alcohols were investigated (Figure 1). A series of reactions with symmetric allylic alcohols containing electron-rich or electron-deficient aryl groups all ran smoothly, providing the corresponding products in moderate to good yields (**3aa**−**3fa**, 63−84%). Meanwhile, unsymmetric allylic alcohols also worked well under standard conditions (**3ga**−**3na**, 45−81% yield). In these cases, two isomers were produced with good selectivities (**3ia**, **3ia′**−**3na**, and **3na′**), which were consistent with Wu and others' works.[11,13] Particularly, allylic alcohol reaction with nitrogen-containing heteroaryls ran smoothly in this procedure, providing the desired product in 41% yield (**3qa**). However, no desired product **3ra** was isolated when using α-aryl-α-cyclic alkyl allylic alcohol.

Next, a series of *sec*-alcohols were tested (Figure 2). 2-Butanol and 2- and 3-pentanol all served as good reaction partners to deliver the corresponding 4,5-diaryl-2,3-dihydrofur-

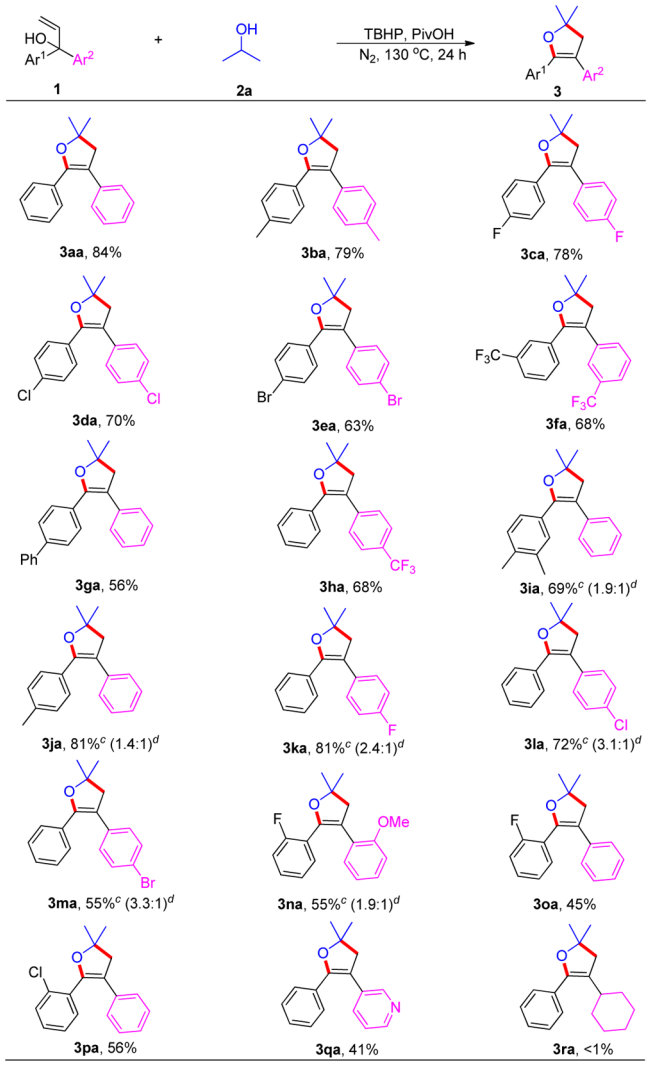


Figure 1. Substrate scope of α,α-diaryl allylic alcohols. [a]Reaction conditions: **1a** (0.2 mmol), **2a** (2 mL), oxidant (0.8 mmol), PivOH (0.02 mmol) at 130 °C under N_2 for 24 h in a sealed tube. [b]Isolated yields. [c]Total yield, only major products are shown. [d]The ratio of **3** was determined by ^{1}H NMR.

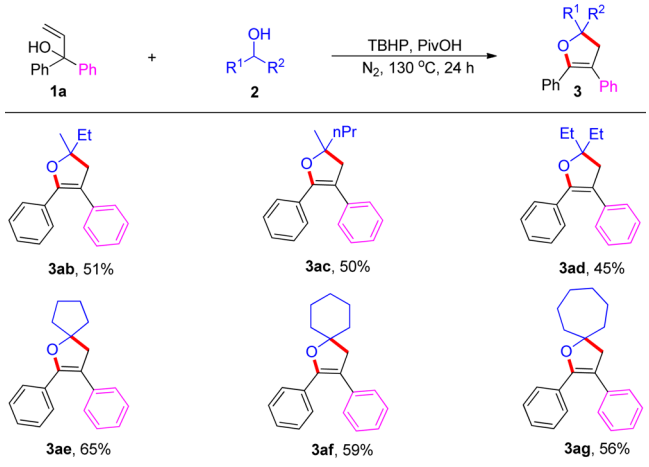


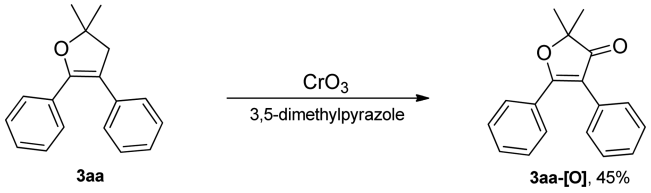
Figure 2. Substrates scope of *sec*-alcohols. Reaction conditions: **1a** (0.2 mmol), **2a** (2 mL), oxidant (0.8 mmol), PivOH (0.02 mmol) at 130 °C under N_2 for 24 h in a sealed tube. Isolated yields.

DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405

ans in moderate yields (**3ab**−**3ad**, 45−51%). Notably, cyclic secondary alcohols also reacted smoothly with allylic alcohols (**3ae**−**3ag**, 56−65%), which offered a novel method to access oxaspiro compounds. Byproduct mainly accounted for the low yields in the cases of **3ma**−**3qa** and **3ab**−**3ad**, like (*E*)-1-bromo-4-(3-isopropoxy-1-phenylallyl)benzene (**3ma** byproduct).

Meanwhile, 2,3-dihydrofurans could be further oxidized to furanones (Scheme 2),[14] which might be applied to the synthesis of bioactive molecules such as 2,2-dimethyl-4-(4-(methylsulfonyl)phenyl)-5-phenylfuran-3(2*H*)-one.[15]

Scheme 2. Allylic Oxidation of 4,5-Diaryl-2,3-dihydrofuran

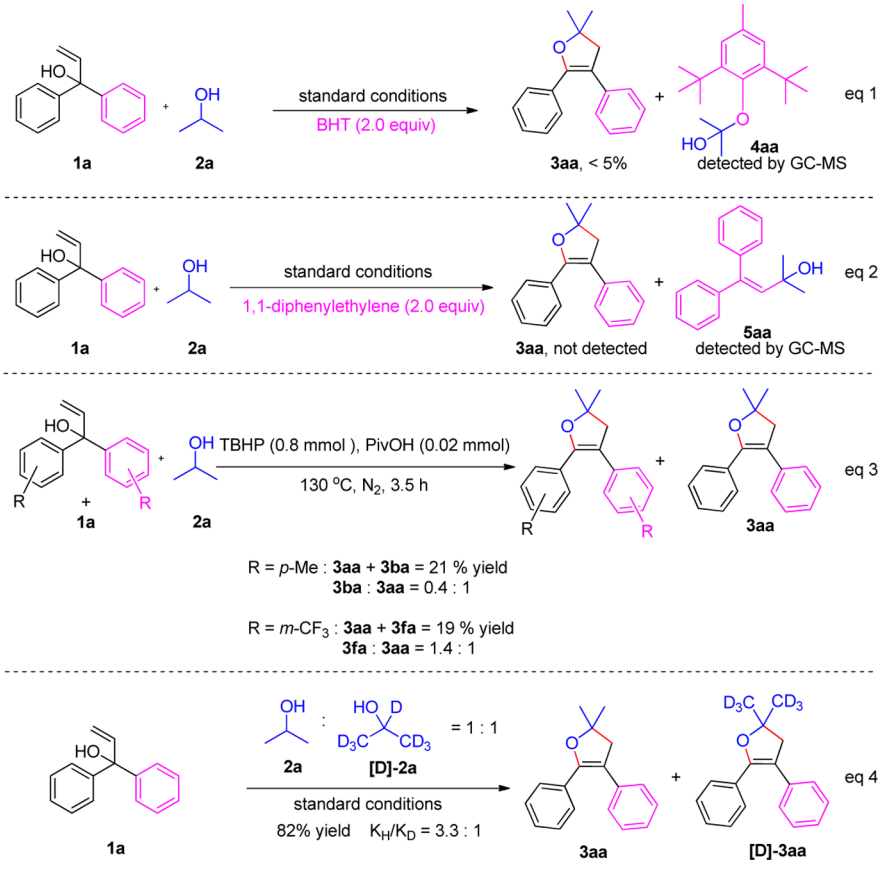


To investigate the mechanism of this reaction, experiments in the presence of the radical-trapping reagents, such as 2,6-di-*tert*-butyl-4-methylphenol (BHT) and 1,1-diphenylethylene, were carried out under standard conditions (Scheme 3, eqs 1 and 2). The formation of desired product **3aa** was suppressed, and adduct products such as **4aa** and **5aa** were observed (by GC-MS). These results indicated that the transformation may proceed via a radical pathway. Next, some competitive experiments were carried out (Scheme 3, eq 3), where the electron-withdrawing group was prone to promote this transformation. This result supported the radical aromatic pathway rather than the electrophilic aromatic substitution.[16] Moreover, an intramolecular rearrangement pathway was determined, supported by the fact that no cross-products were detected (Scheme 3, eq 3). Moreover, the intermolecular competing kinetic isotope effect (KIE) was tested (Scheme 3, eq 4), and a ratio of 3.3:1 for k_H/k_D was observed, which clearly disclosed that the cleavage of the C(sp^3)−H bond may be the rate-determining step in this transformation.

Based on the above results and former reports,[11−13] we proposed a possible mechanism for this reaction (Scheme 4). Initially, with the assistance of TBHP, α-hydroxyisopropyl radical **A** is generated. Subsequently, the addition of radical **A** to allylic alcohol **1a** generates intermediate **B**. Migration of the aryl group via spiro[2,5]octadienyl radical **C** produces intermediate **D**. Then **D** loses an electron with the help of a *tert*-butoxy radical, providing cation intermediate **F**. After that, intramolecular nucleophilic addition takes place, leading to intermediate **G**. Finally, deprotonation and dehydration of intermediate **G** affords the desired product **3aa**.

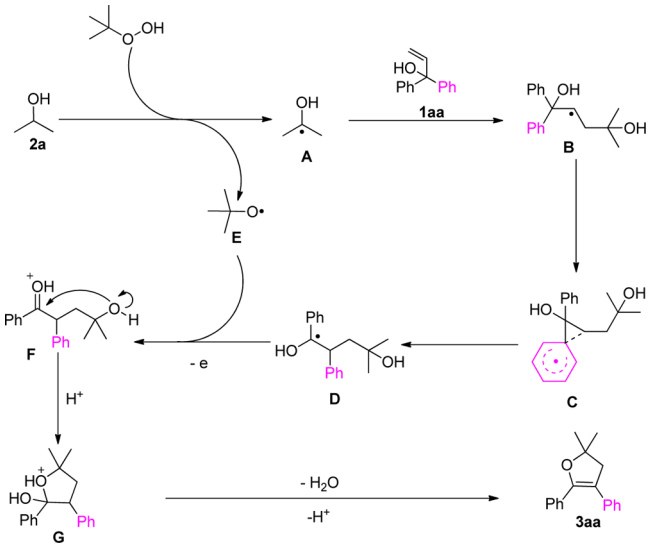
In conclusion, we have developed an unprecedented TBHP-promoted annulation of *sec*-alcohol with α,α-diaryl allylic alcohols, leading to 2,2-dialkyl-4,5-diaryl-2,3-dihydrofuran in moderate to good yields. The procedure involves cascade radical addition and a 1,2-aryl migration process. Notably, phenyl with an electron-withdrawing group migrates preferentially over the aryl substituted with an electron-donating group, while *ortho*-substituted groups are reluctant to migrate. In particular, cyclic secondary alcohols also work well, which offers

Scheme 3. Mechanism Studies



DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405

Scheme 4. Proposed Mechanism



a novel method for the synthesis of spiro compounds. Further allylic oxidation of 2,3-dihydrofurans provides a potential pathway leading to bioactive molecules such as 2,2-dimethyl-4-(4-(methylsulfonyl)phenyl)-5-phenylfuran-3(2*H*)-one.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all chemicals were purchased from commercial suppliers and used without further purification. ^{1}H NMR, ^{13}C NMR, and ^{19}F spectra were recorded at ambient temperature on a 400 or 500 MHz NMR spectrometer (100 MHz for ^{13}C, 125 MHz for ^{13}C DEPT, and 470 MHz for ^{19}F). NMR experiments are reported in δ units, parts per million (ppm), and were referenced to $CDCl_3$ (δ 7.26 or 77.0 ppm) as the internal standard. The coupling constants J are given in hertz. High-resolution mass spectra (HRMS) were obtained using a Bruker micro-TOF II focus spectrometer (ESI). IR spectra were recorded on a spectrometer using KBr discs. Column chromatography was performed using EM silica gel 60 (300−400 mesh).

Experimental Procedure. *Reaction of sec-Alcohols with α,α-Diaryl Allylic Alcohols.* Under N_2, a 20 mL Schlenk tube equipped with a stir bar was charged with α,α-diphenyl allylic alcohol (0.2 mmol), *tert*-butyl hydroperoxide (0.8 mmol), pivalic acid (2.04 mg, 10 mol %), and *sec*-alcohol (2.0 mL). The tube was sealed with a Teflon-lined cap. The reaction mixture was stirred at 130 °C for 24 h in an oil bath. After the completion of the reaction, the solvent was concentrated in vacuum, and the residue was purified by flash column chromatography on silica gel with petroleum ether/EtOAc as the eluent to give the desired product.

Allylic Oxidation of 2,3-Dihydrofuran. Chromium(VI) trioxide (301 mg, 3.01 mmol, 15 equiv) was dried under vacuum over P_2O_5 overnight. To this was added dichloromethane (1.34 mL), and the mixture was cooled to −20 °C using a refrigeration bath. To this cooled solution was added 3,5-dimethylpyrazole (290 mg, 3.01 mmol, 15 equiv) in one portion. The solution was stirred for 30 min at this temperature, at which point the mixture became a brown-red in color. To this was added dihydrofuran **3aa** (50 mg, 0.2 mmol) in dichloromethane (0.7 mL). The mixture was stirred at −20 °C until TLC indicated consumption of starting material (1 h), at which point 5 M NaOH (1.4 mL) was added, and the reaction mixture was warmed to 0 °C and stirred at that temperature for 1 h. The mixture was added into 0.5 M HCl, the layers were separated, the aqueous layer was washed with dichloromethane (2 × 5 mL), and the organics were combined, washed once with brine, dried over $MgSO_4$, filtered through Celite, and concentrated. The crude reaction mixture was purified via column chromatography, yielding furanone **3aa**-[O] (23.8 mg, 45%) as a colorless solid.

*2,2-Dimethyl-4,5-diphenyl-2,3-dihydrofuran (**3aa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3aa** (42.0 mg, 84% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.49 (m, 2H), 7.30 (t, J = 3.2 Hz, 3H), 7.25−7.20 (m, 4H), 7.15−7.11 (m, 1H), 3.02 (s, 2H), 1.55 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.2, 136.3, 132.5, 128.5, 128.14, 128.11, 127.0, 125.6, 108.9, 82.4, 48.3, 28.3; MS (EI) 250 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{19}O$ $(M + H)^+$ 251.1430, found 251.1430; IR (KBr) 3025, 2970, 2926, 2846, 1642, 1599, 1576, 1498, 1445, 1365, 1222 cm^{-1}.

*2,2-Dimethyl-4,5-di-p-tolyl-2,3-dihydrofuran (**3ba**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ba** (44.1 mg, 79% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51−7.49 (m, 2H), 7.30 (t, J = 3.2 Hz, 3H), 7.25−7.20 (m, 4H), 7.15−7.11 (m, 1H), 3.02 (s, 2H), 1.55 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.2, 136.3, 132.5, 128.5, 128.14, 128.11, 127.0, 125.6, 108.9, 82.4, 48.3, 28.3; MS (EI) 278 (M^+); HRMS (ESI) m/z calcd for $C_{20}H_{23}O$ $(M + H)^+$ 279.1743, found 279.1742; IR (KBr) 3085, 3052, 3026, 2980, 2928, 2856, 1646, 1576, 1498, 1465, 1369 cm^{-1}.

*4,5-Bis(4-fluorophenyl)-2,2-dimethyl-2,3-dihydrofuran (**3ca**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ca** (44.6 mg, 78% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46−7.43 (m, 2H), 7.15−7.12 (m, 2H), 7.01−6.90 (m, 4H), 2.97 (s, 2H), 1.53 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.0 (d, J_{C-F} = 169 Hz), 160.1 (d, J_{C-F} = 166 Hz), 150.0 (d, J_{C-F} = 1 Hz), 132.1 (d, J_{C-F} = 3 Hz), 129.9 (d, J_{C-F} = 8 Hz), 128.5 (d, J_{C-F} = 7 Hz), 128.3 (d, J_{C-F} = 3 Hz), 115.3 (d, J_{C-F} = 9 Hz), 1115.1 (d, J_{C-F} = 8 Hz), 107.9, 82.4, 48.5, 28.2; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −112.1, −116.3; MS (EI) 286 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{17}F_2O$ $(M + H)^+$ 287.1242, found 287.1240; IR (KBr) 3052, 2971, 2848, 1646, 1601, 1512, 1447, 1382, 1367, 1256 cm^{-1}.

*4,5-Bis(4-chlorophenyl)-2,2-dimethyl-2,3-dihydrofuran (**3da**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3da** (44.5 mg, 70% yield) as a greenish solid: mp 120−122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.5 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H), 2.95 (s, 2H), 1.51 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 134.5, 134.4, 131.3, 130.5, 129.4, 128.5, 128.4, 128.3, 108.5, 82.8, 48.3, 28.2; MS (EI) 318 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{17}Cl_2O$ $(M + H)^+$ 319.0651, found 319.0650; IR (KBr) 3058, 2928, 2848, 1637, 1591, 1494, 1464, 1444, 1381, 1221 cm^{-1}.

*4,5-Bis(4-bromophenyl)-2,2-dimethyl-2,3-dihydrofuran (**3ea**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ea** (51.0 mg, 63% yield) as a yellowish solid: mp 140−142 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41 (d, J = 8.4 Hz, 2H), 7.34−7.31 (m, 4H), 7.02 (d, J = 8.4 Hz, 2H), 2.95 (s, 2H), 1.51 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 134.9, 131.4, 131.3, 130.9, 130.0, 128.6, 122.7, 119.4, 108.6, 82.3, 48.2, 28.2; ^{13}C NMR (DEPT, $CDCl_3$, 125 MHz) δ 131.5, 131.4, 129.7, 128.7, 48.2, 28.3; MS (EI) 406 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{17}Br_2O$ $(M + H)^+$ 406.9641, found 406.9639; IR (KBr) 3075, 2980, 2972, 2921, 2848, 1653, 1635, 1585, 1490, 1442, 1367, 1220 cm^{-1}.

*2,2-Dimethyl-4,5-bis(3-(trifluoromethyl)phenyl)-2,3-dihydrofuran (**3fa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3fa** (52.5 mg, 68% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (s, 1H), 7.66−7.59 (m, 2H), 7.45−7.34 (m, 5H), 3.08 (s, 2H), 1.58 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.0, 136.5, 132.6, 131.32, 131.32, 130.8 (q, J_{C-F} = 24 Hz), 130.1 (q, J_{C-F} = 2 Hz), 128.8, 128.7, 125.5 (q, J_{C-F} = 4 Hz), 125.0 (q, J_{C-F} = 4 Hz), 123.6 (q, J_{C-F} = 4 Hz), 122.6 (q, J_{C-F} = 4 Hz), 109.2, 83.4, 48.1, 28.2; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −112.2, −116.5; MS (EI) 386 (M^+); HRMS (ESI) m/z calcd for $C_{20}H_{17}F_6O$ $(M + H)^+$ 387.1178, found 387.1175; IR (KBr) 3074, 3045, 2975, 2851, 1645, 1610, 1589, 1492, 1449, 1369, 1252, 1221 cm^{-1}.

*5-([1,1′-Biphenyl]-4-yl)-2,2-dimethyl-4-phenyl-2,3-dihydrofuran (**3ga**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ga** (36.5 mg, 56% yield) as yellowish oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66−7.61 (m, 4H), 7.54−7.47 (m, 4H), 7.38−7.33 (m, 6H), 3.11 (s, 2H), 1.62 (s, 6H); ^{13}C NMR

DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405

($CDCl_3$, 100 MHz) δ 149.6, 140.7, 138.1, 135.3, 132.5, 128.7, 128.6, 128.24, 128.21, 127.2, 127.0, 126.69, 126.68, 108.5, 83.5, 48.1, 28.2; MS (EI) 326 (M^+); HRMS (ESI) m/z calcd for $C_{24}H_{23}O$ $(M + H)^+$ 327.1743, found 327.1740; IR (KBr) 3080, 3055, 3027, 2970, 2926, 2847, 1639, 1598, 1577, 1493, 1366, 1222 cm^{-1}.

*2,2-Dimethyl-5-phenyl-4-(4-(trifluoromethyl)phenyl)-2,3-dihydrofuran (**3ha**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ha** (43.2, 68% yield) as a colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.52−7.50 (m, 2H), 7.46 (d, J = 8.2 Hz, 2H), 7.37−7.36 (m, 3H), 7.28 (d, J = 8.1 Hz, 2H), 3.05 (s, 2H), 1.58 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.6, 140.0, 132.0, 129.1, 128.4, 128.3, 127.4 (q, J_{C-F} = 32 Hz), 125.7, 125.0, (q, J_{C-F} = 3 Hz), 123.0, 107.7, 83.1, 47.7, 28.2; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −62.3; MS (EI) 318 (M^+); HRMS (ESI) m/z calcd for $C_{19}H_{18}F_3O$ $(M + H)^+$ 319.1304, found 319.1303; IR (KBr) 3078, 3050, 2973, 2929, 2851, 1640, 1613, 1599, 1493, 1326, 1261, 1223 cm^{-1}.

*5-(3,4-Dimethylphenyl)-2,2-dimethyl-4-phenyl-2,3-dihydrofuran (**3ia** + **3ia′**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:80) give **3ia** and **3ia′** (38.4 mg, 1.9:1, 69% yield) as a colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.52 (m, 0.72H), 7.31−7.29 (m, 1.75H), 7.22 (d, J = 4.2 Hz, 3.08H), 7.14−7.11 (m, 0.61H), 7.07−6.95 (m, 1.81H), 3.01 (s, 1.29H), 3.00 (s, 0.67H), 2.28 (s, 1.92H), 2.24 (s, 3H), 2.20 (s, 1.09H), 1.54 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.6, 148.4, 137.0, 136.44, 136.37, 136.2, 133.9, 133.8, 132.6, 130.0, 129.40, 129.36, 129.1, 128.24, 128.19, 128.04, 128.02, 128.00, 126.8, 125.7, 125.3, 124.5, 109.0, 108.1, 82.14, 82.11, 48.6, 48.2, 28.3, 28.2, 19.7, 19.7, 19.6, 19.4; MS (EI) 278 (M^+); HRMS (ESI) m/z calcd for $C_{20}H_{23}O$ $(M + H)^+$ 279.1743, found 279.1741; IR (KBr) 3075, 3054, 3023, 2969, 2923, 2849, 1641, 1599, 1504, 1445, 1366, 1258, 1216 cm^{-1}.

*2,2-Dimethyl-4-phenyl-5-(p-tolyl)-2,3-dihydrofuran (**3ja** + **3ja′**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:80) give the product **3ja** and **3ja′** (42.8 mg, 1.4:1, 81% yield) as a colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.57−7.55 (m, 0.79H), 7.45 (d, J = 8.0 Hz, 1.25H), 7.35−7.33 (m, 1.33H), 7.27 (d, J = 4.3 Hz, 2.58H), 7.16 (d, J = 6.6 Hz, 2.7H), 7.09 (d, J = 8.0 Hz, 0.87H), 3.06 (s, 1.17H), 3.05 (s, 0.84H), 2.41 (s, 1.75H), 2.37 (s, 1.25H), 1.59 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.4, 148.5, 138.3, 136.4, 135.2, 133.3, 132.5, 130.0, 128.8, 128.3, 128.07, 128.06, 128.04, 128.01, 126.9, 125.4, 108.9, 108.2, 82.2, 48.5, 48.2, 28.2, 21.3, 21.1; MS (EI) 264 (M^+); HRMS (ESI) m/z calcd for $C_{19}H_{21}O$ $(M + H)^+$ 265.1587, found 265.1587; IR (KBr) 3055, 3027, 2970, 2924, 2851, 1643, 1599, 1513, 1445,1366,1257, 1222 cm^{-1}.

*4-(4-Fluorophenyl)-2,2-dimethyl-5-phenyl-2,3-dihydrofuran (**3ka** + **3ka′**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ka** and **3ka′** (43.4 mg, 2.4:1, 81% yield) as colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.55−7.51 (m, 2H), 7.35−7.17 (m, 5H), 7.05−6.94 (m, 2.04H), 3.06 (s, 1.41H), 3.03 (s, 0.59H), 1.59 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 162.6 (d, J_{C-F} = 147 Hz), 160.9 (d, J_{C-F} = 243 Hz), 149.0 (d, J_{C-F} = 1 Hz), 148.1 (d, J_{C-F} = 1 Hz), 136.1, 132.2 (d, J_{C-F} = 2 Hz), 130.0 (d, J_{C-F} = 8 Hz), 128.5, 128.4 (d, J_{C-F} = 4 Hz), 128.2, 128.0, 127.0, 125.7, 115.1 (d, J_{C-F} = 21 Hz), 115.0 (d, J_{C-F} = 12 Hz), 108.9 (d, J_{C-F} = 1 Hz), 107.9, 82.42, 82.32, 48.4, 48.3, 28.23, 28.19 ; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −112.2, −116.5; MS (EI) 268 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{18}FO$ $(M + H)^+$ 269.1336, found 269.1335; IR (KBr) 3082, 3054, 2971, 2926, 2847, 1644, 1600, 1510, 1445, 1357, 1231 cm^{-1}.

*4-(4-Chlorophenyl)-2,2-dimethyl-5-phenyl-2,3-dihydrofuran (**3la** + **3la′**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3la** and **3la′** (40.9 mg, 3.1:1, 72% yield) as a greenish oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.50−7.44 (m, 2.16H), 7.34−7.32 (m, 2.84H), 7.21−7.18 (m, 2.36H), 7.13−7.11 (d, J = 8.6 Hz, 1.58H), 3.02 (s, 0.49H), 2.99 (s, 1.51H), 1.56 (s, 4.12H), 1.55 (s, 1.89H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.0, 147.8, 135.9, 135.2, 132.1, 131.3, 131.1, 130.0, 128.7, 128.4, 128.3, 128.2, 128.1, 127.1, 125.9, 122.3, 118.9, 109.8, 107.8, 88.6, 88.5, 48.5, 48.0, 28.22, 28.20; MS (EI) 284 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{18}ClO$ $(M + H)^+$ 285.1041, found 285.1042; IR (KBr) 3079, 3055, 3025, 2971, 2926, 2847, 1641, 1599, 1496, 1445, 1367, 1258 cm^{-1}.

*4-(4-Bromophenyl)-2,2-dimethyl-5-phenyl-2,3-dihydrofuran (**3ma** + **3ma′**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ma** and **3ma′** (36.1 mg, 3.3:1, 55% yield) as a yellowish oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.49−7.47 (t, J = 3.58 Hz, 3.58H), 7.43−7.36 (m, 1.09H), 7.32 (d, J = 6.7 Hz, 3.81H), 7.26−7.16 (m, 1.21 H), 7.05 (d, J = 8.3 Hz, 1.48H), 3.00 (s, 0.46H), 2.98 (s, 1.50H), 1.54 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.0, 147.8, 135.9, 135.2, 132.1, 131.3, 131.1, 130.6, 129.7, 128.7, 128.4, 128.27, 128.25, 128.1, 127.1, 125.9, 122.3, 118.9, 109.8, 107.8, 82.6, 82.5, 48.5, 48.0, 28.22, 28.20; MS (EI) 328 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{18}BrO$ $(M + H)^+$ 329.0536, found 329.0533; IR (KBr) 3086, 3056, 3025, 2970, 2926, 2847, 1640, 1599, 1495, 1445, 1367, 1258, 1222 cm^{-1}.

*4-(2-Fluorophenyl)-5-(4-methoxyphenyl)-2,2-dimethyl-2,3-dihydrofuran (**3na** + **3na′**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:50) give **3na** and **3na′** (32.8 mg, 1.9:1, 55% yield) as a colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.45 (t, J = 7.3 Hz, 0.35H), 7.38−7.32 (m, 1.46H), 7.22−7.15 (m, 1.63H), 7.09−6.98 (m, 2.52H), 6.79−6.74 (m, 2.05H), 3.78 (s, 1.91H), 3.77 (s, 1.09H), 3.02 (s, 0.68H), 3.00 (s, 1.30H), 1.56 (s, 1.92H), 1.54 (s, 3.98H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.5, 161.4, 159.5, 159.1, 158.9, 157.4, 151.1, 142.9, 131.1 (d, J_{C-F} = 3 Hz), 130.9 (d, J_{C-F} = 4 Hz), 130.4 (d, J_{C-F} = 8 Hz), 128.8, 128.0, 127.6 (d, J_{C-F} = 8 Hz), 126.8, 124.6 (d, J_{C-F} = 14 Hz), 124.4. 124.1 (d, J_{C-F} = 3 Hz), 123.8 (d, J_{C-F} = 3 Hz), 121.2 (d, J_{C-F} = 14 Hz), 116.1 (d, J_{C-F} = 21 Hz), 115.8 (d, J_{C-F} = 21 Hz), 113.5, 113.3, 118.2, 102.3, 83.0, 82.3, 55.09, 55.08, 48.5, 47.1, 28.2, 28.0; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −99.69; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −111.5, 112.2; MS (EI) 298 (M^+); HRMS (ESI) m/z calcd for $C_{19}H_{20}FO_2$ $(M + H)^+$ 299.1442, found 299.1442; IR (KBr) 3075, 3061, 3038, 2970, 2930, 2838, 1647, 1607, 1575, 1513, 1486, 1367, 1247 cm^{-1}.

*4-(2-Fluorophenyl)-2,2-dimethyl-5-phenyl-2,3-dihydrofuran (**3oa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3oa** (24.1 mg, 45% yield) as a colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.41 (m, 2H), 7.25 (d, J = 5.1 Hz, 3H), 7.19 (t, J = 7.4 Hz, 2H), 7.08−6.99 (m, 2H), 3.02 (s, 2H), 1.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.3 (d, J_{C-F} = 246 Hz), 150.3, 131.9, 130.9, (d, J_{C-F} = 4 Hz), 128.3, 127.9, 127.8, (d, J_{C-F} = 8 Hz), 127.4, 124.4 (d, J_{C-F} = 15 Hz), 123.8 (d, J_{C-F} = 3 Hz), 115.8 (d, J_{C-F} = 22 Hz), 103.9, 83.1, 48.6, 28.1; ^{19}F NMR ($CDCl_3$, 470 MHz) δ −112.3; MS (EI) 268 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{18}FO$ $(M + H)^+$ 269.1336, found 269.1336; IR (KBr) 3078, 3058, 2970, 2921, 2850, 1647, 1600, 1497, 1447, 1367, 1264, 1216 cm^{-1}.

*4-(2-Chlorophenyl)-2,2-dimethyl-5-phenyl-2,3-dihydrofuran (**3pa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3pa** (31.8 mg, 56% yield) as a colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.5 (d, J = 7.9 Hz, 1H), 7..41−7.34 (m, 2H), 7.30 (t, J = 7.4 Hz, 1H), 7.18 (t, J = 7.5 Hz, 2H), 7.09 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 7.7 Hz, 2H), 3.08 (s, 2H), 1.60 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.7, 135.0, 134.2, 132.3, 131.5, 131.2, 131.0, 128.0, 127.0, 125.4, 125.2, 110.8, 83.8, 46.3, 28.3; MS (EI) 284 (M^+); HRMS (ESI) m/z calcd for $C_{18}H_{18}ClO$ $(M + H)^+$ 285.1041, found 285.1040; IR (KBr) 3081, 3056, 3029, 2971, 2926, 2849, 1654, 1598, 1494, 1442, 1367, 1250, 1222 cm^{-1}.

*3-(5,5-Dimethyl-2-phenyl-4,5-dihydrofuran-3-yl)pyridine (**3qa**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:5) give **3qa** (20.6 mg, 41% yield) as a yellowish oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 8.41 (s, 1H), 8.32 (d, J = 4.6 Hz, 1H), 7.45−7.43 (m, 3H), 7.31 (d, J = 5.4 Hz, 3H), 7.10−7.07 (m, 1H), 3.00 (s, 2H), 1.54 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.2, 148.0, 146.4, 133.7, 132.2, 131.8, 129.0, 128.5, 128.1, 122.9, 105.4, 96.8, 83.1, 47.5, 28.3; MS (EI) 251 (M^+); HRMS (ESI) m/z calcd for $C_{17}H_{18}NO$ $(M + H)^+$ 252.1383, found 252.1386; IR (KBr) 3069, 3053, 3026, 2986, 2922, 2850, 1635, 1599, 1494, 1367, 1260 cm^{-1}.

*2-Ethyl-2-methyl-4,5-diphenyl-2,3-dihydrofuran (**3ab**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ab** (26.9 mg, 51% yield) as colorless oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.51(m, 2H), 7.32 (t, J = 3.1 Hz, 3H), 7.24−7.23 (m. 4H), 7.18−7.12 (m, 1H), 3.08 (d, J = 14.8 Hz, 1H), 2.94 (d, J = 14.8 Hz, 1H), 1.83 (q, J = 7.4 Hz, 2H), 1.51 (s, 3H), 1.08

DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405

(t, J = 7.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.4, 136.3, 132.5, 128.4, 128.14, 128.13, 128.1, 126.9, 125.5, 108.8, 84.8, 46.0, 33.9, 26.1, 8.4; MS (EI) 264 (M^+); HRMS (ESI) m/z calcd for $C_{19}H_{21}O$ $(M + H)^+$ 265.1587, found 265.1587; IR (KBr) 3080, 3054, 3024, 2968, 2925, 2848, 1644, 1599, 1498, 1445, 1374, 1244 cm^{-1}.

*2-Methyl-4,5-diphenyl-2-propyl-2,3-dihydrofuran (**3ac**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ac** (27.8 mg, 50% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.51 (m, 2H), 7.31 (t, J = 3.1 Hz, 3H), 7.25−7.23 (m, 4H), 7.18−7.12 (m, 1H), 3.09 (d, J = 14.8 Hz, 1H), 2.95 (d, J = 14.8 Hz, 1H), 1.81−1.77 (m, 2H), 1.60−1.54 (m, 2H), 1.52 (s, 3H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.0, 136.2, 132.5, 128.4, 128.12, 128.1, 127.0, 125.5, 108.8, 84.5, 46.6, 43.7, 26.6, 17.4, 14.6; MS (EI) 278 (M^+); HRMS (ESI) m/z calcd for $C_{20}H_{23}O$ $(M + H)^+$ 279.1743, found 279.1742; IR (KBr) 3080, 3055, 3025, 2959, 2930, 2871, 2848, 1644, 1600, 1497, 1445, 1373, 1242 cm^{-1}.

*2,2-Diethyl-4,5-diphenyl-2,3-dihydrofuran (**3ad**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ad** (25.0 mg, 45% yield) as colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 (d, J = 2.4 Hz, 2H), 7.31 (d, J = 2.8 Hz, 3H), 7.25−7.31 (m, 4H), 7.15−7.13 (m, 1H), 2.98 (s, 2H), 1.8 (q, J = 7.4 Hz, 4H), 1.4 (t, J = 7.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.8, 136.2, 132.5, 128.4, 128.2, 128.12, 128.09, 127.0, 125.5, 108.9, 87.0, 43.6, 31.7, 7.9; MS (EI) 278 (M^+); HRMS (ESI) m/z calcd for $C_{20}H_{23}O$ $(M + H)^+$ 279.1743, found 279.1739; IR (KBr) 3077, 3054, 3024, 2965, 2921, 2878, 2851, 1647, 1599, 1499, 1459, 1377, 1246 cm^{-1}.

*2,3-Diphenyl-1-oxaspiro[4.4]non-2-ene (**3ae**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ae** (35.9 mg, 65% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53−7.51 (m, 2H), 7.32−7.30 (m, 3H), 7.24−7.23 (m, 4H), 7.17−7.12 (m, 1H), 3.20 (s, 2H), 2.25 (m, 2H), 1.99−1.92 (m, 2H), 1.83−1.78 (m, 4H), 1.52 (s, 3H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.4, 136.2, 132.4, 128.4, 128.2, 128.11, 128.08, 126.9, 125.5, 109.3, 92.7, 45.8, 39.6, 23.9; MS (EI) 276 (M^+); HRMS (ESI) m/z calcd for $C_{20}H_{21}O$ $(M + H)^+$ 277.1587, found 277.1588; IR (KBr) 3080, 3054, 3023, 2958, 2923, 2871, 2848, 1640, 1599, 1497, 1445, 1357, 1246 cm^{-1}.

*2,3-Diphenyl-1-oxaspiro[4.5]dec-2-ene (**3af**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3af** (34.2 mg, 59% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.39 (m, 2H), 7.19−7.17 (m, 3H), 7.13−7.10 (m, 4H), 7.06−6.98 (m, 1H), 2.85 (s, 2H), 1.85−1.78 (m, 2H), 1.75−1.59 (m, 4H), 1.45−1.36 (m, 4H), 1.02 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 136.4, 132.5, 128.4, 128.2, 128.1, 126.9, 125.5, 108.6, 84.1, 46.6, 37.1, 25.3, 23.0; MS (EI) 290 (M^+); HRMS (ESI) m/z calcd for $C_{21}H_{23}O$ $(M + H)^+$ 291.1743, found 291.1742; IR (KBr) 3070, 3054, 3025, 2968, 2929, 2873, 2848, 1650, 1596, 1490, 1455, 1357, 1256 cm^{-1}.

*2,3-Diphenyl-1-oxaspiro[4.6]undec-2-ene (**3ag**).* Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:100) give **3ag** (30.0 mg, 56% yield) as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42−7.39 (m, 2H), 7.21−7.18 (m, 3H), 7.12−7.10 (m, 4H), 7.05−7.00 (m, 1H), 2.90 (s, 2H), 2.07−1.99 (m, 2H), 1.87−1.83 (m, 1H), 1.67−1.44 (m, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 136.4, 132.5, 128.4, 128.2, 128.11, 128.08, 126.9, 125.4, 108.5, 87.8, 48.2, 40.5, 28.8, 22.1; MS (EI) 304 (M^+); HRMS (ESI) m/z calcd for $C_{22}H_{25}O$ $(M + H)^+$ 305.1900, found 305.1889; IR (KBr) 3086, 3063, 2958, 2923, 2871, 2846, 1649, 1589, 1496, 1445, 1353, 1259 cm^{-1}.

*2,2-Dimethyl-4,5-diphenylfuran-3(2H)-one (**3aa-[O]**).*[17] Flash column chromatography on silica gel (ethyl acetate/petroleum ether 1:30) give **3aa-[O]** (23.8.0 mg, 45% yield) as a colorless solid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.66−7.63 (m, 2H), 7.49−7.44 (m, 1H), 7.38−7.30 (m, 7H), 1.56 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 205.5, 178.2, 131.8, 130.0, 129.5, 128.6, 128.4, 127.5, 113.6.4, 87.0, 23.4; MS (EI) 264 (M^+).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00643.

Experimental details on the mechanism study, along with copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra of compounds **3aa**−**3qa**, **3ab**−**3ag**, and **3aa-[O]** (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: jiangcheng@cczu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (Nos. 21272028, 21572025, and 21202013), "Innovation & Entrepreneurship Talents" Introduction Plan of Jiangsu Province, the Key University Science Research Project of Jiangsu Province (15KJA150001), Qing Lan Project of Jiangsu Province, Jiangsu Key Laboratory of Advanced Catalytic Materials & Technology (BM2012110), and Advanced Catalysis and Green Manufacturing Collaborative Innovation Center for financial support.

■ REFERENCES

(1) Selective examples: (a) Meyers, A. I. *Heterocycles in Organic Synthesis*; John Wiley & Sons: New York, 1974. (b) Dean, F. M. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., Ed.; Academic: New York, 1982; Vol. *30*, pp 167−238. (c) Dean, F. M.; Sargent, M. V. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Cheeseman, G. W. H., Eds.; Pergamon: New York, 1984; Vol. *4*, Part 3, pp 531−598. (d) Vernin, G. *The Chemistry of Heterocyclic Flavoring and Aroma Compounds*; Ellis Horwood: Chichester, UK, 1982.

(2) Selective examples: (a) Kilroy, T. G.; O'Sullivan, T. P.; Guiry, P. J. *Eur. J. Org. Chem.* **2005**, *2005*, 4929. (b) Evans, D. A.; Sweeney, Z. K.; Rovis, T.; Tedrow, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 12095. (c) Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407. (d) Fraga, B. M. *Nat. Prod. Rep.* **1992**, *9*, 217. (e) Merritt, A. T.; Ley, S. V. *Nat. Prod. Rep.* **1992**, *9*, 243. (f) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795. (g) Yu, J.-T.; Shi, B.; Peng, H.; Sun, S.; Chu, H.; Jiang, Y.; Cheng, J. *Org. Lett.* **2015**, *17*, 3643.

(3) Selective examples: (a) Hou, X.-L.; Yang, Z.; Yeung, K.-S.; Wong, H. N. C. *Prog. Heterocycl. Chem.* **2005**, *17*, 142. (b) Faul, M. M.; Huff, B. E. *Chem. Rev.* **2000**, *100*, 2407. (c) Mueller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Grass, S. *Synlett* **2005**, 1397. (d) Ishitani, H.; Achiwa, K. *Heterocycles* **1997**, *46*, 153.

(4) (a) Spencer, T. A.; Villarica, R. M.; Storm, D. L.; Weaver, T. D.; Friary, R. J.; Posler, J.; Shafer, P. R. *J. Am. Chem. Soc.* **1967**, *89*, 5497. (b) Arai, S.; Nakayama, K.; Suzuki, Y.; Hatano, K.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 9739. (c) Anac, O.; Ozdemir, A. D.; Sezer, O. *Helv. Chim. Acta* **2003**, *86*, 290. (d) Jiang, Y.; Ma, D. *Tetrahedron: Asymmetry* **2002**, *13*, 1033. (e) Son, S.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 1046.

(5) (a) Aso, M.; Ojida, A.; Yang, G.; Cha, O. J.; Osawa, E.; Kanematsu, K. *J. Org. Chem.* **1993**, *58*, 3960. (b) Antonioletti, R.; Righi, G.; Oliveri, L.; Bovicelli, P. *Tetrahedron Lett.* **2000**, *41*, 10127. (c) Antonioletti, R.; Bovicelli, P.; Malancona, S. *Tetrahedron* **2002**, *58*, 589. (d) Lee, Y. R.; Suk, J. Y. *Tetrahedron* **2002**, *58*, 2359.

(6) For some selected examples, see: (a) Ichikawa, K.; Uemura, S. *J. Org. Chem.* **1967**, *32*, 493. (b) Tategami, S.; Yamada, T.; Nishino, H.; Korp, J. D.; Kurosawa, K. *Tetrahedron Lett.* **1990**, *31*, 6371. (c) Baciocchi, E.; Ruzziconi, R. *J. Org. Chem.* **1991**, *56*, 4772. (d) McDonald, F. E.; Connolly, C. B.; Gleason, M. M.; Towne, T. B.;

DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405

Treiber, K. D. *J. Org. Chem.* **1993**, *58*, 6952. (e) Evans, D. A.; Sweeney, Z. K.; Rovis, T.; Tedrow, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 12095. (f) Zhang, Y.; Raines, A. J.; Flowers, R. A. *Org. Lett.* **2003**, *5*, 2363.
(7) (a) Calo, V.; Scordari, F.; Nacci, A.; Schingaro, E.; D'Accolti, L.; Monopoli, A. *J. Org. Chem.* **2003**, *68*, 4406. (b) Xing, C.; Zhu, S. *J. Org. Chem.* **2004**, *69*, 6486.
(8) Chen, J.; Chen, C.; Chen, J.; Wang, G.; Qu, H. *Chem. Commun.* **2015**, *51*, 1356.
(9) Wang, J.; Yao, X.; Wang, T.; Han, J.; Zhang, J.; Zhang, X.; Wang, P.; Zhang, Z. *Org. Lett.* **2015**, *17*, 5124.
(10) Selective examples: (a) Zhou, W.; Qian, P.; Zhao, J.; Fang, H.; Han, J.; Pan, Y. *Org. Lett.* **2015**, *17*, 1160. (b) Meng, Y.; Guo, L.-N.; Wang, H.; Duan, X.-H. *Chem. Commun.* **2013**, *49*, 7540. (c) Shi, L.; Tu, Y.-Q.; Wang, M.; Zhang, F.-M.; Fan, Ch.-A.; Zhao, Y.-M.; Xia, W.-J. *J. Am. Chem. Soc.* **2005**, *127*, 10836. (d) Correia, C. A.; Yang, L.; Li, C.-J. *Org. Lett.* **2011**, *13*, 4581. (e) Cui, Z.; Shang, X.; Shao, X.-F.; Liu, Z.-Q. *Chem. Sci.* **2012**, *3*, 2853. (f) Liu, Zh.-Q.; Sun, L.; Wang, J.-G.; Han, J.; Zhao, Y.-K.; Zhou, B. *Org. Lett.* **2009**, *11*, 1437. (g) He, T.; Yu, L.; Zhang, L.; Wang, L.; Wang, M. *Org. Lett.* **2011**, *13*, 5016. (h) Jiang, Y.-J.; Tu, Y.-Q.; Zhang, E.; Zhang, S.-Y.; Cao, K.; Shi, L. *Adv. Synth. Catal.* **2008**, *350*, 552. (i) Zhang, S.-Y.; Tu, Y.-Q.; Fan, C.-A.; Zhang, F.-M.; Shi, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 8761.
(11) (a) Liu, X.; Xiong, F.; Huang, X.; Xu, L.; Li, P.; Wu, X. *Angew. Chem., Int. Ed.* **2013**, *52*, 6962. (b) Xu, P.; Hu, K.; Gu, Z.; Cheng, Y.; Zhu, C. *Chem. Commun.* **2015**, *51*, 7222. (c) Chu, X.-Q.; Meng, H.; Zi, Y.; Xu, X.-P.; Ji, S.-J. *Chem. - Eur. J.* **2014**, *20*, 17198.
(12) (a) Majetich, G.; Wheless, K. *Tetrahedron* **1995**, *51*, 7095. (b) Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203. (c) Ammann, S. E.; Rice, G. T.; White, M. C. *J. Am. Chem. Soc.* **2014**, *136*, 10834. (d) Thompson, S. J.; Thach, D. Q.; Dong, G. *J. Am. Chem. Soc.* **2015**, *137*, 11586.
(13) Bunescu, A.; Wang, Q.; Zhu, J. *Angew. Chem., Int. Ed.* **2015**, *54*, 3132.
(14) Mack, D. J.; Njardarson, J. T. *Angew. Chem., Int. Ed.* **2013**, *52*, 1543.
(15) (a) Shin, S. S.; Noh, M.-S.; Byun, Y. J.; Choi, J. K.; Kim, J. Y.; Lim, K. M.; Ha, J.-Y.; Kim, J. K.; Lee, C. H.; Chung, S. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 165. (b) Lee, K.-W.; Choi, Y. H.; Joo, Y. H.; Kim, J. K.; Shin, S. S.; Byun, Y. J.; Kim, Y.; Chung, S. *Bioorg. Med. Chem.* **2002**, *10*, 1137. (c) Shin, S. S.; Byun, Y.; Lim, K. M.; Choi, J. K.; Lee, K.-W.; Moh, J. H.; Kim, J. K.; Jeong, Y. S.; Kim, J. Y.; Choi, Y. H.; Koh, H.-J.; Park, Y.-H.; Oh, Y. I.; Noh, M.-S.; Chung, S. *J. Med. Chem.* **2004**, *47*, 792.
(16) (a) Ruchardt, C.; Hecht, R. *Chem. Ber.* **1965**, *98*, 2471. (b) Studer, A.; Bossart, M. *Tetrahedron* **2001**, *57*, 9649. (c) AurelianoAntunes, C. S.; Bietti, M.; Ercolani, G.; Lanzalunga, O.; Salamone, M. *J. Org. Chem.* **2005**, *70*, 3884.
(17) Rodina, L. L.; Medvedev, J. J.; Galkina, O. S.; Nikolaev, V. A. *Eur. J. Org. Chem.* **2014**, *2014*, 2993.

DOI: 10.1021/acs.joc.6b00643
J. Org. Chem. 2016, 81, 4399−4405