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A Metal-Free Tandem C–C/C–O Bond Formation Approach to Diversely Functionalized Tetrasubstituted Furans

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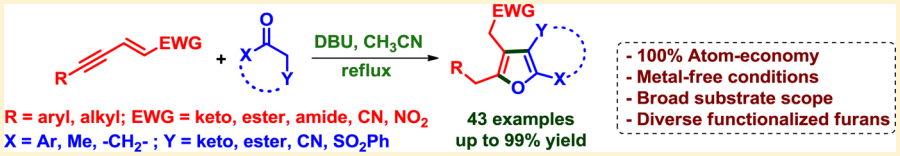
Supporting Information



ABSTRACT: A novel and efficient method for the synthesis of diversely functionalized furans is developed via DBU-mediated tandem Michael addition/5-*exo*-*dig*-cycloisomerization of enynes and keto-methylenes. This [3 + 2]-annulation is operationally simple under metal-free reaction conditions with 100% atom economy and broad substrate scope.

INTRODUCTION

The development of an atom-economical approach for the efficient construction of diversely functionalized molecules from easily accessible starting materials is continuously a special attention for synthetic organic chemists.[1] Furan is one of the extensively studied oxygenated heterocycles because of its broad occurrence in many natural products,[2] pharmaceuticals,[3] and functional materials.[4] For example, two sesquiterpenoids (**I** and **II**) isolated from the mycelia of edible mushroom *Pleurotus cornucopiae* fermented on rice,[2i] the pukalide class of molecules (**III**),[2e] and angelone (**IV**)[2d] are some of the representative natural products possessing substituted furan skeleton (Figure 1). Several of the natural furans have shown exciting biological activities, such as anticancer, antidiabetic, and antiallergic activities, etc.[2] In addition, substituted furans are also useful building blocks in organic synthesis.[5]

Consequently, substantial consideration has been paid on the advance of effective methods to synthesize these heterocyclic compounds after the discovery of traditional condensation of 1,4-dicarbonyl compound reactions (Paal–Knorr synthesis).[6] During the past decade, numerous alternative approaches have been developed, and predominantly these reactions are either alkyne- or allene-assisted cyclizations.[7−14] Among the alkyne-based strategies to polysubstituted furans, cyclizations of enynones are particularly attractive (Scheme 1). For instance, enynedione compounds were successfully utilized to prepare trisubstituted furans (path A) through the intramolecular cyclization.[9] In 2004, Larock and co-workers demonstrated 2-(1-alkynyl)-2-alkene-1-ones as suitable starting materials for substituted furans via gold-catalyzed cyclization.[10a,b] Later, these enynones were vastly explored for the synthesis of diversely functionalized furans by several research groups in the presence of various metal catalysts (path B).[10c−n] Notably, Zhang and co-workers have vastly explored the efficacy of 2-(1-

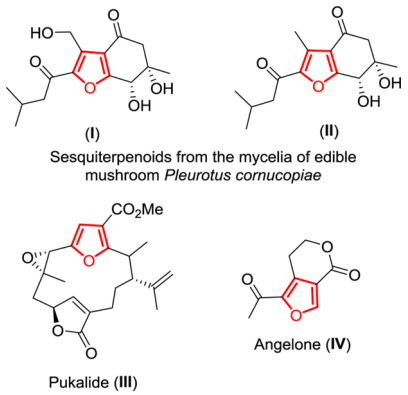
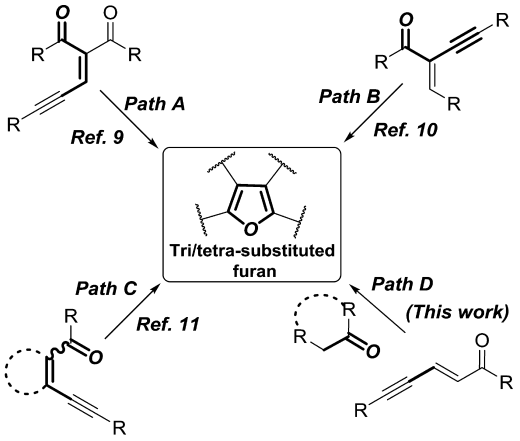


Figure 1. Structures of representative natural products having furan framework.

Scheme 1. Furan Synthesis from Enynones



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alkynyl)-2-alkene-1-ones in the synthesis of diversely substituted furnans.[10g−n] In addition, 2-alken-4-yn-1-ones (mostly in *Z*-form) were also used to synthesize substituted furans (path C).[11]

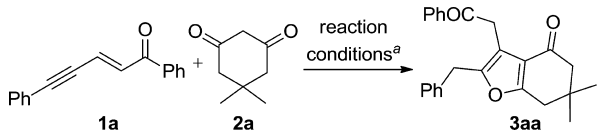
While a majority of the above cyclizations required metal catalyst to promote the carbon−oxygen bond formation, metal-free reactions from these enynones are rather scarce.[11e,f] Further, in all the above methods, the substitutions on the furan ring originated from the enynone, which contribute 4-carbons and oxygen through the intramolecular cyclization. Herein, we report a metal-free intermolecular cyclization strategy for the synthesis of tetrasubstituted furans from enynones (C2 synthon), which allows diverse substitutions on the furan ring (path D).

Following our current interest in alkyne-based strategies toward heterocycles,[15] we envisioned a new [3 + 2] annulation comprising the Michael addition of keto-active methylene on to 2-alken-4-yn-1-one would provide the 1,4-ynone, which subsequently undergo the 5-*exo*-*dig*-cycloisomerization for the construction of tetrasubstituted furans. We also envisaged that the process would occur in one pot and possesses more potential in the synthesis of diversely functionalized furans, as the substrates are accessible with a range of groups. To our knowledge, the intermolecular version using enynones has not been reported (path D), in which two different substrates can combine in one step to form furan ring, potentially with higher diversity.

RESULTS AND DISCUSSION

To test the hypothesis, we began the investigation by treatment of enynone **1a** with 5,5-dimethyl-1,3-cyclohexanedione (**2a**) in presence of K_2CO_3 in dichloromethane, which provided the expected furan **3aa** in 40% yield (entry 1, Table 1). Despite low conversion, this first result showed the feasibility of the envisioned strategy. Encouraged by this result, we further examined the same reaction under various conditions to improve the product yield. The use of K_2CO_3 in acetonitrile helped in improving the yield to 54% (entry 2, Table 1). The

Table 1. Preliminary Optimization Studies



1a 2a 3aa

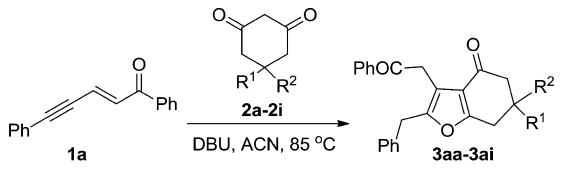
entry	base/equiv	solvent	time (h)	yield (%)[b]
1	K_2CO_3/2	CH_2Cl_2	30	40
2	K_2CO_3/2	CH_3CN	24	54
3	CS_2CO_3/2	CH_3CN	24	41
4	DABCO/1	CH_3CN	24	59
5	DMAP/1	CH_3CN	24	34
6	DBU/2	CH_3CN	14	86
7	**DBU/1**	**CH_3CN**	**15**	**98**
8	DBU/0.5	CH_3CN	20	91
9	DBU/0.2	CH_3CN	30	86
10	DBU/0.1	CH_3CN	30	81
11	DBU/1	toluene	14	94
12	DBU/1	dioxane	14	90
13	DBU/1	THF	26	79

[a]Reaction conditions: **1a** (1.0 mmol), 5,5-dimethylcyclohexane-1,3-dione **2a** (1.1 mmol) in solvent (9 mL) at reflux temperature. [b]Yields of the isolated products after chromatography.

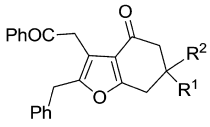
screening of bases (Cs_2CO_3, DABCO, DMAP and DBU) for the reaction of **1a** with **2a** revealed that DBU is the base of choice in affording the 86% yield of **3aa** (entries 3 to 6, Table 1). Additional optimization revealed that variation in the amount of DBU employed or changing the solvent has little influence on the outcome of the reaction (entries 7 to 13, Table 1). Thus, the optimized procedure for the tandem Michael addition/5-*exo*-*dig*-cycloisomerization was chosen as follows: the reaction was carried out in acetonitrile in presence of 1 equiv of DBU at refluxing conditions (entry 7, Table 1). It is noteworthy to mention that the reaction at room temperature provided the Michael addition product **A**,[16] and when the temperature raised to reflux, the desired furan was accomplished.

After optimizing the reaction conditions, generality of the present [3 + 2]-annulation reaction was investigated. Thus, a series of substiuted 1,3-cyclohexanediones treated with enynone **1a**, as summarized in Scheme 2. Several 1,3-

Scheme 2. Scope of Cyclic 1,3-Diketones in Furan Synthesis[a]



1a 3aa-3ai



3aa (R^1 = Me, R^2 = Me, 15 h, 98%)

3ab (R^1 = H, R^2 = H, 16 h, 93%)

3ac (R^1 = Me, R^2 =H, 15 h, 97%)

3ad (R^1 = Isopropyl, R^2 = H, 19 h, 91%)

3ae (R^1 = Phenyl, R^2 = H, 16 h, 99%)

3af (R^1 = 4-*OMe*-phenyl, R^2 = H, 15 h, 97%)

3ag (R^1 = 4-*N*(Me)$_2$-phenyl, R^2 = H, 16 h, 99%)

3ah (R^1 = benzo[*d*][1,3]dioxol-4-yl, R^2 = H,15 h, 97%)

3ai (R^1 = 2-Furyl, R^2 = H, 15 h, 82%)

[a]Reaction conditions: **1a** (1.0 mmol), cyclic 1,3-dione **2** (1.1 mmol), DBU (1.0 mmol), CH_3CN (9 mL), at 85 °C.

cyclohexanediones, having C5-alkyl (products **3ab** and **3ad**) or C5-aryl substitution (products **3ae** to **3ai**), were smoothly participated in the tandem reaction to provide the corresponding furans in excellent yields (Scheme 2).

Next, the developed tandem reaction was tested with other keto-active methylenes, and the results are summarized in Table 2. Acyclic 1,3-diketones such as pentane-2,4-dione (**2j**) and 1,3-diphenylpropane-1,3-dione (**2k**) were also employed in the reaction to afford furans **3aj** and **3ak** in 71% and 95% yields (entries 1 and 2, Table 2), respectively. Further, *β*-keto esters also turned out to be excellent substrates in the present method to afford substituted furans **3al** to **3an** in good yields (entries 3−5, Table 2). Interestingly, 3-oxo-3-arylpropanenitriles **2o**−**2t** underwent [3 + 2]-annulation with **1a** to give the corresponding 2-aryl-3-cyano furans **3ao**−**3at** in good yield (entries 6−11, Table 2). Additionally *β*-keto Sulphone **2u** was also found to be compatible in the tandem reaction with **1a** affording **3au** in 73% yield (entry 12, Table 2). It is worth

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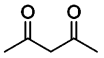
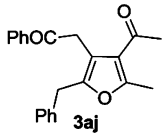
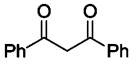
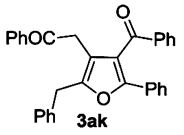
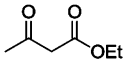
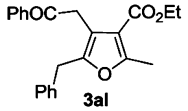
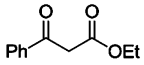
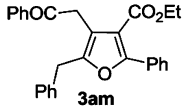
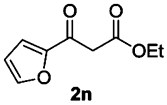
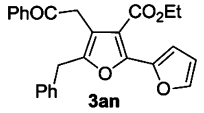
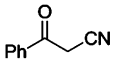
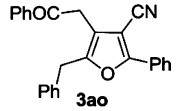
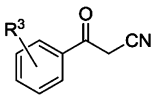
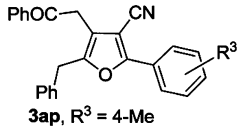
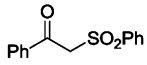
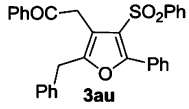
Table 2. Reaction of 1a with Acyclic Keto-Active Methylenes[b]

Entry	Keto-active methylene	Time (h)	Product (3)	Yield[a]
1	 **2j**	15	 **3aj**	71
2	 **2k**	20	 **3ak**	95
3	 **2l**	15	 **3al**	67
4	 **2m**	15	 **3am**	79
5	 **2n**	20	 **3an**	76
6	 **2o**	19	 **3ao**	89
7	 **2p**, R^3 = 4-Me	17	 **3ap**, R^3 = 4-Me	88
8	**2q**, R^3 = 4-OMe	15	**3aq**, R^3 = 4-OMe	91
9	**2r**, R^3 = 3-Cl	18	**3ar**, R^3 = 3-Cl	86
10	**2s**, R^3 = 4-CO_2Me	18	**3as**, R^3 = 4-CO_2Me	79
11	**2t**, R^3 = 4-F	16	**3at**, R^3 = 4-F	72
12	 **2u**	20	 **3au**	73

[a]Isolated yields. [b]Reaction conditions: Enynone **1a** (1.0 mmol), keto-active methylene **2** (1.1 mmol), DBU (1.0 mmol), CH_3CN (9 mL), 85 °C.

noting that only one example is known in the literature for the synthesis of 3-cyano or 3-sulfonyl furans from alkynones.[9c]

Subsequently, the scope of the reaction was studied with enynones possessing different substitutions on the alkyne functionality under the optimized conditions (Table 3). A wide range of 5-aryl-1-phenylpent-2-en-4-yn-1-ones, **1b**−**1h**, comprising either an eletron-donating or electron-withdrawing subtituted phenyl group on the alkyne, were found to be suitable for the present [3 + 2]-annulation providing the corresponding furans **3ba**−**3ha** in excellent yields (entries 1−7, Table 3). Other enynones with 1-naphthyl (**1i**) or 2-thiophenyl (**1j**) substitution on the alkyne were also found to be excellent substrates in yielding the furans **3ia** and **3ja** in 97 and 96% yields, respectively (entries 8 and 9, Table 3). Gratifyingly, enynones **1k** and **1l** with alkyl substitution on the alkyne functionality also furnsihed the substitued furans **3ka** and **3la** (entries 10 and 11, Table 3) in good yields.

After successfully optimizing the conditions for the synthesis of substituted furans with various structurally diverse enynones and 1,3-diketones, we turned our attention in the use of substrates containing diverse electron-withdrawing groups in conjugation to enyne (Scheme 3). Accordingly, reaction of **1m** possessing an unsaturated ketone with **2a** was verified under DBU/CH_3CN conditions, and to our satisfaction, the formation of furan **3ma** (96%) was observed. Similarly, enynes comprising an unsaturated esters (**1n** and **1o**) or amide (**1p**) were also found to be well-suited substrates for the tandem reaction with **2a** to afford the corresponding furans **3na**−**3pa**, respectively, in high yield. Interestingly, enynes containing cyano (**1q**) or nitro (**1r**) substitution on the olefin also reacted with the 1,3-diketone **2a** to yield **3qa** (84%) and **3ra** (81%). To the best of our knowledge, synthesis of substituted furans from the enynes **1p**−**1r** hitherto is not reported, and this study comprises the first example of such study. Reaction of enyne having conjugation to cyclic ketone (**1s**) with **2a** proceeded

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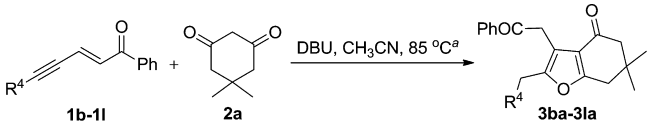
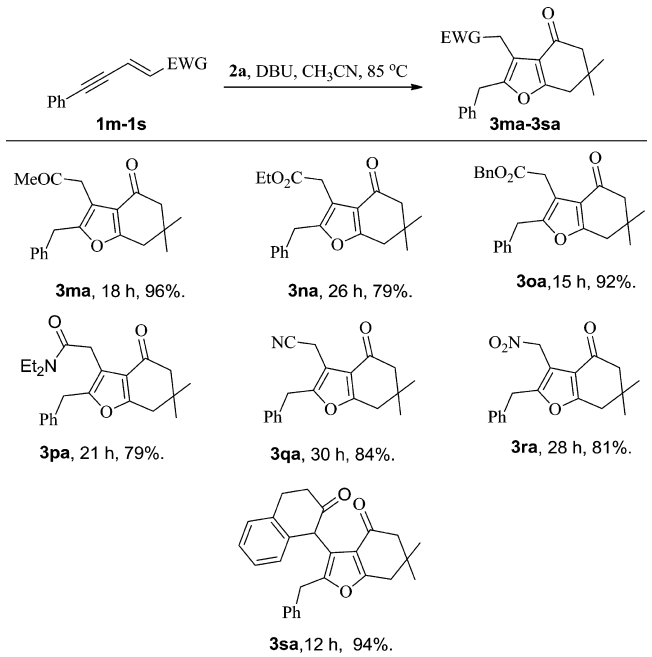
Table 3. Scope of Substitution on Alkyne Terminus of Enynone



entry	enyne (**1**)	time (h)	furan (**3**)	yield (%)[b]
1	R^4 = 4-Me-Ph, **1b**	20	**3ba**	95
2	R^4 = 4-MeO-Ph, **1c**	18	**3ca**	97
3	R^4 = 2,4-di-MeO-Ph, **1d**	21	**3da**	90
4	R^4 = 3-CF_3-Ph, **1e**	23	**3ea**	95
5	R^4 = 4-Cl-Ph, **1f**	20	**3fa**	96
6	R^4 = 2-I-Ph, **1g**	20	**3ga**	96
7	R^4 = 4-NO_2-Ph, **1h**	20	**3ha**	86
8	R^4 = 1-Napthyl, **1i**	18	**3ia**	97
9	R^4 = 2-Thiophenyl, **1j**	22	**3ja**	96
10	R^4 = Ph—CH═CH, **1k**	22	**3ka**	90
11	R^4 = nC_8H_{17}, **1l**	24	**31a**	74

[a]Reaction conditions: Enynone **1** (1.0 mmol), **2a** (1.1 mmol), DBU (1.0 mmol), CH_3CN (9 mL), 85 °C. [b]Isolated yields.

Scheme 3. Reactions of Enynes Linked with Different Electron-Withdrawing Groups[a]

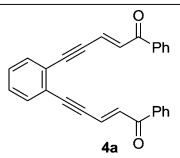
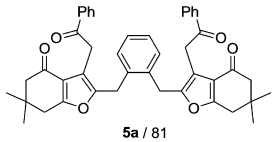
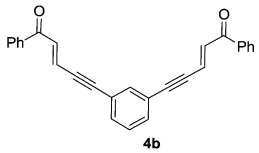
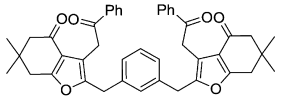
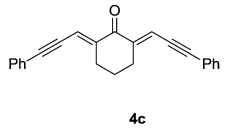
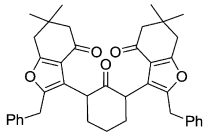
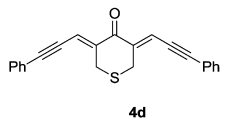
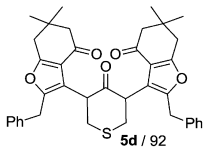


[a]Reaction conditions: Enyne **1** (1.0 mmol), **2a** (1.1 mmol) CH_3CN (9 mL), at 85 °C. Yields are given for the isolated products after chromatography.

well to give the furan **3sa** in 94% yield. The above results clearly demonstrate the additional diversity of the reaction in obtaining the furans with various functionalities, which are handy for further transformations.

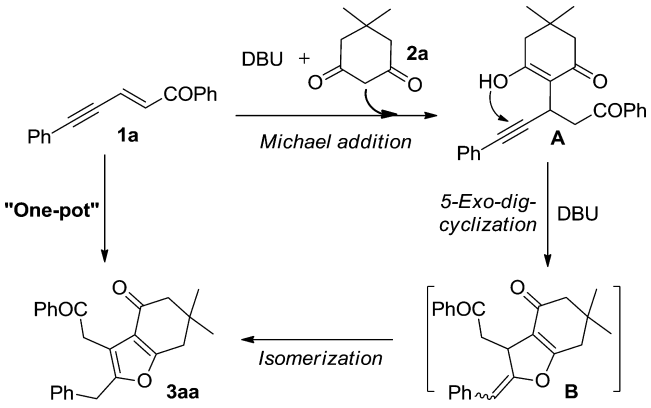
Finally, versatality of the reaction was explored with substrates having either two enynone frameworks tethered to phenyl ring (**4a** and **4b**) or two enyne units based on cyclic ketone (**4c** and **4d**). Thus, reaction of **4a**−**4d** with 1,3-diketone **2a** furnished the corresponding bis-furanyl derivatives **5a**−**5d** in good yields (entries 1 to 4, Table 4).

Table 4. Synthesis of Bis-furan Moieties[b]

Entry	Enyne	Product / Yield (%)[a]
1	 4a	 5a / 81
2	 4b	 5b / 89
3	 4c	 5c / 93
4	 4d	 5d / 92

[a]Isolated yields. [b]Reaction conditions: Entnone (0.4 mmol), **2a** (0.84 mmol), DBU (0.8 mmol), CH_3CN (9 mL), 85 °C for 20 h.

Scheme 4. Proposed Mechanism for the C−C/C−O Bond Formation



A possible mechanism is outlined in Scheme 4. We believe that the Michael addition of active-methylene **2a** to the conjugated ketone **1a** (C−C bond formation) in the presence of base (DBU) offers the intermediate **A**, which exists as enol form. Subsequently, intermediate **A** undergoes 5-*exo*-*dig*-cyclization (C−O bond formation) to give **B**, followed by isomerization of the double bond, leading to the formation of furan **3aa**. A substantial support for this mechanism was evidence by the isolation and characterization of intermediate **A**,[16] which independently on treatement with DBU afforded the furan **3aa**. It is important to mention that the intermediate **A** type precursors for the synthesis of furans have been made earlier from propargylic alcohols through the nucleophilic substitution reaction.[17] However, the substrates were limited to the propargylic alcohols flanked on one side by an aryl (phenyl) group and on the other side with an acetylenic group. Moreover, the use of acid catalyst (in majority cases metal catalyst) is essential for nucleophilic substitution reaction

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between propargylic alcohol and a dicarbonyl compound or enoxysilane. In contrast, the present method offers the intermediate **A** from enynones through Michael addition reaction, which expand the choice of substitutions on furan ring, and the simple base is sufficient to promote the formation of precursor **A** as well as cyclization to furan.

In summary, we have developed a novel DBU-promoted [3 + 2]-annulation reaction for the synthesis of substituted furans involving of (*E*)-2-alken-4-yn-1-ones with keto-active methylenes. The reaction was shown to proceed through a tandem Michael addition/5-*exo*-*dig*-cycloisomerization. The present protocol is efficient for varied substituted enynes as well as several active methylenes including cyclic and acyclic 1,3-diketones, β-keto esters, nitriles, and sulfone. Salient features of this operationally simple protocol are metal-free reaction conditions, 100% atom economy, and broad substrate scope to obtain diversely functionalized furans. Importantly, several functional groups such as keto, ester, amide, sulfone, nitro and cyano groups could be installed on the furan ring, thus providing opportunities for further elaboration of the products.

EXPERIMENTAL SECTION

General Methods. Reactions were monitored by thin-layer chromatography carried out on silica plates using UV-light and anisaldehyde or potassium permanganate or β-naphthol for visualization. Column chromatography was performed on silica gel (60−120 mesh) using *n*-hexane and ethyl acetate as eluent. Evaporation of solvents was conducted under reduced pressure at temperatures less than 45 °C. FTIR spectra were recorded on KBr thin film. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on a 300, 500, and 600 MHz NMR spectrometer. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz), respectively. Chemical shifts are reported relative to residual solvent as an internal standard for ^{1}H and ^{13}C ($CDCl_3$ δ 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). Mass spectra were obtained on VG 70−70H or LC/MSD trapSL spectrometer operating at 70 eV using direct inlet system.

Substituted enynes **1a−1q** have been prepared using the literature procedure,[18,11e,f] compounds **1s**, **4c**, and **4d** have been prepared using the literature procedure,[19] and known compounds data have been compared with the reported data. Characterization data for new compounds is given below.

General Procedure for the Preparation of Substituted Enynes (1a−1q). To a solution of acetylenic aldehyde (5.0 mmol) in 20 mL of THF was added corresponding Wittig ylide (5.5 mmol) at 0 °C. The reaction mixture was stirred at the room temperature for 12 h. After the completion of reaction, the mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding product.

*(E)-1-Phenyl-5-(p-tolyl)pent-2-en-4-yn-1-one (**1b**).* 1.13 g, 92% yield, brown solid: mp 66−67 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, J = 6.8, 1.5 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.54−7.39 (m, 5H), 7.18 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 15.8 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.2, 139.5, 136.9, 132.8, 132.3, 131.7, 129.0, 128.4, 128.3, 124.8, 118.9, 99.7, 87.3, 21.2; IR (KBr) ν_{max} = 3057, 2919, 2185, 1652, 1577, 1443, 1330, 1253, 995, 812, 689 cm^{-1}; MS (ESI) m/z 247 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{18}H_{15}O$ (M + H)$^+$ 247.1117, found 247.1115.

*(E)-5-(4-Methoxyphenyl)-1-phenylpent-2-en-4-yn-1-one (**1c**).* 1.16 g, 89% yield, yellow solid: mp 160−162 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, J = 6.8, 1.5 Hz, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.54−7.45 (m, 4H), 7.41 (d, J = 15.9 Hz, 1H), 7.14 (d, J = 15.9 Hz, 1H), 6.90 (d, J = 6.8 Hz, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.5, 160.4, 137.1, 133.5, 132.8, 131.8, 128.4, 128.3, 125.3, 114.0, 100.0, 87.0, 72.4, 55.0; IR (KBr) ν_{max} = 2957, 2933, 2866, 2188, 1649, 1576, 1463, 1333, 1254, 1018, 824, 689 cm^{-1}; MS (ESI) m/z 263 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{18}H_{15}O_2$ (M + H)$^+$ 263.1066, found 263.1059.

*(E)-5-(3,5-Dimethoxyphenyl)-1-phenylpent-2-en-4-yn-1-one (**1d**).* 1.37 g, 94% yield, yellow solid: mp 86−88 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, J = 7.2, 1.4 Hz, 2H), 7.58 (t, J = 7.3 Hz, 1H), 7.49 (t, J = 7.3 Hz, 2H), 7.41 (d, J = 8.5 Hz, 1H), 7.39 (d, J = 15.5 Hz, 1H), 7.19 (d, J = 15.5 Hz, 1H), 6.49 (dd, J = 8.4, 2.4 Hz, 1H), 6.45 (d, J = 2.4 Hz, 1H), 3.90 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.8, 162.2, 161.6, 137.3, 134.9, 132.9, 131.4, 128.5, 128.3, 105.1, 98.2, 97.0, 91.1, 55.7, 55.3; IR (KBr) ν_{max} = 3052, 2957, 2836, 2184, 1654, 1580, 1464, 1334, 1209, 1161, 958, 826, 684 cm^{-1}; MS (ESI) m/z 293 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{19}H_{17}O_3$ (M + H)$^+$ 293.1172, found 293.1171.

*(E)-1-Phenyl-5-(3-(trifluoromethyl)phenyl)pent-2-en-4-yn-1-one (**1e**).* 1.26 g, 84% yield, pale yellow crystals: mp 80−81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, J = 8.2, 1.5 Hz, 2H), 7.79 (s, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.65−7.59 (m, 2H), 7.54−7.47 (m, 4H), 7.11 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.1, 136.8, 134.8, 133.7, 133.1, 131.5, 128.9, 128.5, 128.3, 125.6, 125.6, 123.8, 123.0, 121.6, 96.7, 88.8; IR (KBr) ν_{max} = 3060, 2926, 2197, 1660, 1591, 1441, 1344, 1298, 1118, 950, 805, 690 cm^{-1}; MS (ESI) m/z 301 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{18}H_{12}OF_3$ (M + H)$^+$ 301.0834, found 301.0829.

*(E)-5-(4-Chlorophenyl)-1-phenylpent-2-en-4-yn-1-one (**1f**).* 1.25 g, 94% yield, pale yellow solid: mp 93−94 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.2, 1.4 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.47−7.43 (m, 3H), 7.37−7.34 (m, 2H), 7.11 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.6, 137.2, 135.6, 133.4, 133.3, 133.2, 128.9, 128.7, 128.6, 124.6, 120.8, 97.9, 88.7; IR (KBr) ν_{max} = 3060, 2919, 2195, 1652, 1574, 1483, 1332, 1256, 1005, 968, 826, 695 cm^{-1}; MS (ESI) m/z 267 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{17}H_{12}OCl$ (M + H)$^+$ 267.0571, found 267.0562.

*(E)-5-(2-Iodophenyl)-1-phenylpent-2-en-4-yn-1-one (**1g**).* 1.57 g, 88% yield, pale yellow crystals: mp 70−71 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.1, 1.5 Hz, 2H), 7.89 (dd, J = 8.1, 1.1 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.54−7.49 (m, 4H), 7.35 (td, J = 7.6, 1.1 Hz, 1H), 7.16 (d, J = 15.4 Hz, 1H), 7.07 (td, J = 7.8, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.7, 138.8, 137.0, 133.5, 133.2, 133.0, 130.4, 128.7, 128.6, 128.5, 127.9, 124.6, 101.2, 100.6, 90.9; IR (KBr) ν_{max} = 2925, 2192, 1656, 1591, 1568, 1438, 1330, 1248, 999, 753, 689 cm^{-1}; MS (ESI) m/z 359 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{17}H_{12}OI$ (M + H)$^+$ 358.9927, found 358.9925.

*(E)-5-(4-Nitrophenyl)-1-phenylpent-2-en-4-yn-1-one (**1h**).* 1.18 g, 85% yield, pale yellow solid: mp 130−132 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (dd, J = 9.0, 1.8 Hz, 2H), 8.01 (d, J = 8.2 Hz, 2H), 7.67 (dd, J = 8.7, 1.5 Hz, 2H), 7.62 (t, J = 8.4 Hz, 1H), 7.55−7.50 (m, 3H), 7.12 (d, J = 15.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.2, 147.4, 136.7, 134.5, 133.4, 132.6, 131.8, 128.7, 128.4, 123.6, 123.4, 95.8, 91.9; IR (KBr) ν_{max} = 3068, 2924, 2195, 1649, 1515, 1444, 1336, 1251, 854, 692 cm^{-1}; MS (ESI) m/z 279 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{17}H_{12}O_3N$ (M + H)$^+$ 279.0889, found 279.0885.

*(E)-5-(Naphthalen-1-yl)-1-phenylpent-2-en-4-yn-1-one (**1i**).* 1.30 g, 92% yield, pale yellow solid: mp 85−86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (d, J = 8.3 Hz, 1H), 8.04 (dd, J = 6.8, 1.5 Hz, 2H), 7.89 (t, J = 6.8 Hz, 2H), 7.77 (d, J = 8.3 Hz, 1H), 7.66−7.48 (m, 7H), 7.25 (d, J = 15.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.5, 137.0, 133.0, 132.8, 131.3, 129.9, 128.6, 128.5, 128.4, 128.3, 127.0, 126.5, 125.7, 125.1, 124.8, 121.2, 119.7, 97.5, 92.5; IR (neat) ν_{max} = 3055, 2919, 2185, 1657, 1592, 1447, 1270, 1008, 950, 768, 689 cm^{-1}; MS (ESI) m/z 283 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{21}H_{15}O$ (M + H)$^+$ 283.1117, found 283.1112.

*(E)-1-Phenyl-5-(thiophen-2-yl)pent-2-en-4-yn-1-one (**1j**).* 1.13 g, 95% yield, brown solid: mp 77−78 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.4, 1.4 Hz, 2H), 7.60 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 7.42 (d, J = 15.6 Hz, 1H), 7.40 (dd, J = 5.2, 1.2 Hz, 1H), 7.35 (dd, J = 3.7, 1.2 Hz, 1H), 7.14 (d, J = 15.6 Hz, 1H), 7.05 (dd, J = 5.2, 3.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.3, 136.9, 133.7, 132.1, 129.3, 128.9, 128.5, 128.3, 127.4, 124.3, 122.0, 96.7, 92.2; IR (KBr) ν_{max} = 3105, 2172, 1652, 1581, 1415, 1358, 1295, 1200, 1013,

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953, 703 cm^{-1}; MS (ESI) m/z 239 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{15}H_{11}OS$ $(M + H)^+$ 239.0525, found 239.0519.

*(2E,6E)-1,7-Diphenylhepta-2,6-dien-4-yn-1-one (**1k**).* 1.02 g, 79% yield, brown solid: mp 95−96 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.50 (t, J = 7.3 Hz, 2H), 7.44 (d, J = 7.0 Hz, 2H), 7.41−7.39 (m, 4H), 7.14−7.07 (m, 2H), 6.38 (d, J = 16.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.5, 143.8, 137.0, 135.5, 132.9, 132.5, 129.2, 128.6, 128.5, 128.3, 126.5, 124.9, 107.2, 99.2, 90.3; IR (KBr) ν_{max} = 3057, 2923, 2168, 1653, 1564, 1445, 1372, 1255, 995, 819, 695 cm^{-1}; MS (ESI) m/z 259 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{19}H_{15}O$ $(M + H)^+$ 259.1117, found 259.1110.

*(E)-1-Phenyltridec-2-en-4-yn-1-one (**1l**).* 1.19 g, 89% yield, pale yellow liquid: ^1H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, J = 8.5, 1.4 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.48 (t, J = 7.3 Hz, 2H), 7.27 (d, J = 15.6 Hz, 1H), 6.90 (dt, J = 15.6, 2.3 Hz, 1H), 2.42 (td, J = 7.2, 2.3 Hz, 2H), 1.61−1.55 (m, 2H), 1.45−1.38 (m, 2H), 1.34−1.25 (m, 8H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.9, 137.2, 132.8, 132.4, 128.5, 128.3, 126.2, 102.0, 79.2, 31.7, 29.0, 28.9, 28.8, 28.3, 22.5, 19.8, 14.0; IR (neat) ν_{max} = 2925, 2854, 2210, 1661, 1592, 1450, 1287, 1009, 959, 693 cm^{-1}; MS (ESI) m/z 269 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{19}H_{25}O$ $(M + H)^+$ 269.1899, found 269.1897.

*(E)-Benzyl 5-phenylpent-2-en-4-ynoate (**1o**).* 1.21 g, 93% yield, white solid: mp 65−66 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, J = 8.1, 1.5 Hz, 2H), 7.39−7.28 (m, 8H), 7.02 (d, J = 15.7 Hz, 1H), 6.35 (d, J = 15.7 Hz, 1H), 5.22 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 135.6, 131.8, 129.5, 129.2, 128.5, 128.3, 128.2, 128.1, 127.6, 125.5, 98.6, 86.2, 66.4; IR (KBr) ν_{max} = 3064, 3033, 2954, 2198, 1715, 1617, 1311, 1252, 1164, 959, 754, 692 cm^{-1}; MS (ESI) m/z 263 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{18}H_{15}O2$ $(M + H)^+$ 263.1067, found 263.1060.

Synthesis of (*E*)-2-(3-Phenylprop-2-yn-1-ylidene)-3,4-dihydronaphthalen-1(2*H*)-one (1s). To a solution of 3-phenylpropiolaldehyde (5.0 mmol) in 20 mL of THF:H_2O (8:2) was added 3,4-dihydronaphthalen-1(2*H*)-one (5.0 mmol) and NaOH (5.0 mmol), stirred at 0 °C for 3 h. After the completion of reaction, the mixture was diluted with H_2O (20 mL) and extracted with EtOAc (10 mL × 2); organic layer was washed with H_2O, brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the title compound **1s** (1.05 g, 81% yield) as a white solid: mp 75−77 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (dd, J = 7.8, 1.1 Hz, 1H), 7.55−7.48 (m, 3H), 7.39−7.34 (m, 4H), 7.28 (d, J = 7.6 Hz, 1H), 7.02 (t, J = 1.7 Hz, 1H), 3.16 (td, J = 6.9, 1.5 Hz, 2H), 3.04 (d, J = 6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.8, 144.7, 143.8, 133.4, 132.9, 131.7, 129.0, 128.4, 128.3, 128.0, 127.0, 122.6, 116.6, 102.2, 86.9, 28.4, 28.2; IR (KBr) ν_{max} = 3050, 2952, 2185, 1657, 1590, 1447, 1270, 1008, 768, 689 cm^{-1}; MS (ESI) m/z 259 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{19}H_{15}O$ $(M + H)^+$ 259.1117, found 259.1115.

General Procedure for the Preparation of Substituted Enyne (4a, 4b). To a solution of diacetylenic aldehyde (3.0 mmol) in 20 mL of THF was added corresponding Wittig ylide (6.6 mmol) at 0 °C. The reaction mixture was stirred at the room temperature for 3 h. After the completion of reaction, the mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding product (**4a**, **4b**).

*(2E,2′E)-5,5′-(1,2-Phenylene)bis(1-phenylpent-2-en-4-yn-1-one) (**4a**).* 0.60 g, 62% yield, brown solid: mp 218−219 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (dd, J = 8.7, 1.5 Hz, 1H), 7.67 (dd, J = 8.5, 1.3 Hz, 2H), 7.39−7.06 (m, 12H), 6.79 (s, 1H), 6.92 (d, J = 15.5 Hz, 1H), 6.87 (d, J = 15.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.6, 137.0, 134.5, 133.7, 132.4, 131.0, 129.2, 128.8, 128.5, 124.7, 97.2, 92.1; IR (neat) ν_{max} = 3057, 2921, 2851, 2189, 1656, 1588, 1446, 1255, 999, 951, 760, 689 cm^{-1}; MS (ESI) m/z 387 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{28}H_{19}O_2$ $(M + H)^+$ 387.1380, found 387.1375.

*(2E,2′E)-5,5′-(1,3-Phenylene)bis(1-phenylpent-2-en-4-yn-1-one) (**4b**).* 0.68 g, 69% yield, brown solid: mp 188−189 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.5, 1.3 Hz, 4H), 7.70−7.35 (m, 12H), 7.12 (d, J = 15.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.7, 137.1, 135.3, 133.6, 133.3, 132.6, 128.7, 128.6, 128.5, 124.6, 122.9, 97.6, 88.5; IR (neat) ν_{max} = 2921, 2851, 2190, 1651, 1594, 1445, 1215, 1011, 958, 691 cm^{-1}; MS (ESI) m/z 387 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{28}H_{19}O_2$ $(M + H)^+$ 387.1380, found 387.1378.

General Procedure for the Preparation of 4c and 4d. To a solution of 3-phenylpropiolaldehyde (5.0 mmol) in 20 mL of THF:H_2O (8:2) was added cyclic ketone (cyclohexanone or dihydro-2*H*-thiopyran-4(3*H*)-one), (2.5 mmol) and NaOH (3.0 mmol), stirred at 0 °C for 2 h. After the completion of reaction, the mixture was diluted with H_2O (20 mL) and extracted with EtOAc (10 mL × 2); organic layer was washed with H_2O, brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding product (**4c**, **4d**).

*(2E,6E)-2,6-Bis(3-phenylprop-2-yn-1-lidene)cyclohexanone (**4c**).* 0.52 g, 65% yield, brown solid: mp 146−147 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55−7.46 (m, 4H), 7.41−7.31 (m, 6H), 6.98 (s, 2H), 2.93 (td, J = 7.5, 1.9 Hz, 4H), 1.93−1.81 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 186.2, 145.3, 131.8, 129.1, 128.4, 122.6, 118.2, 103.8, 87.3, 28.9, 21.6; IR (KBr) ν_{max} = 3054, 2937, 2871, 2189, 1658, 1597, 1577, 1440, 1308, 1173, 902, 756, 687 cm^{-1}; MS (ESI) m/z 323 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{24}H_{19}O$ $(M + H)^+$ 323.1430, found 323.1424.

*(3Z,5Z)-3,5-Bis(3-phenylprop-2-yn-1-ylidene)dihydro-2H-thiopyran-4(3H)-one (**4d**).* 0.53 g, 62% yield, brown solid: mp 96−98 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54−7.47 (m, 4H), 7.43−7.32 (m, 6H), 6.99 (s, 2H), 3.94 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.7, 141.7, 131.9, 129.4, 128.4, 122.2, 118.1, 104.7, 86.4, 30.9; IR (KBr) ν_{max} = 3050, 2951, 2859, 2191, 1657, 1593, 1447, 1211, 1014, 950, 691 cm^{-1}; MS (ESI) m/z 341 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{23}H_{17}OS$ $(M + H)^+$ 341.0994, found 341.0995.

3-Hydroxy-5,5-dimethyl-2-(5-oxo-1,5-diphenylpent-1-yn-3-yl)cyclohex-2-enone (A). To a solution of **1** (1.0 mmol) in 9 mL of acetonitrile was added ketomethylene **2** (1.1 mmol) and DBU (1.0 mmol) at room temperature and stirred for 3 h. After the completion of reaction, the mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the title compound **A** in 96% yield (357 mg), as a brown solid: ^1H NMR (500 MHz, $CDCl_3$) δ 9.90 (br s, 1H), 8.00 (dd, J = 7.3, 1.2 Hz, 2H), 7.63−7.37 (m, 6H), 7.31−7.22 (m, 2H), 4.69 (t, J = 4.9 Hz, 1H), 3.66 (dd, J = 18.3, 5.0 Hz, 1H), 3.42 (dd, J = 18.5, 4.6 Hz, 1H), 2.40 (d, J = 6.9 Hz, 2H), 2.23 (s, 2H), 1.08 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 196.9, 172.5, 135.9, 133.8, 131.7, 128.7, 128.3, 128.2, 128.1, 122.8, 112.4, 88.5, 83.5, 50.4, 43.5, 43.0, 31.3, 28.6, 27.8, 22.0; IR (KBr) ν_{max} = 3409, 3034, 2957, 2854, 2191, 1711, 1653, 1580, 1401, 1265, 1107, 985, 760 cm^{-1}; MS (ESI) m/z 395 $(M + Na)^+$; HRMS (ESI) m/z calcd for $C_{25}H_{24}O_3Na$ $(M + Na)^+$ 395.1617, found 395.1614.

General Procedure for the Synthesis of Tetrasubstituted Furans (3). To a solution of **1** (1.0 mmol) in 9 mL of acetonitrile was added keto-active methylene **2** (1.1 mmol) and DBU (1.0 mmol) at room temperature, and the mixture was then heated to 85 °C and stirred for 8−30 h. After the completion of reaction, the mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding product.

*2-Benzyl-6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3aa**).* 364 mg, 98% yield, white solid: mp 118−119 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 7.7 Hz, 2H), 7.54 (dd, J = 7.7, 6.6 Hz, 1H), 7.44 (t, J = 7.7 Hz, 2H), 7.25 (dd, J = 7.7, 6.6 Hz, 2H), 7.20−7.16 (m, 3H), 4.28 (s, 2H), 3.94 (s, 2H), 2.70 (s, 2H), 2.32 (s, 2H), 1.15 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 194.8, 165.1, 152.0, 137.2, 136.7, 132.9, 128.48, 128.46, 128.4, 128.3, 126.5, 119.1, 111.3, 52.2, 37.3, 35.1, 33.5, 32.1, 28.5; IR (KBr) ν_{max} = 3061, 2958, 2931, 1671, 1589, 1453, 1350, 1216, 1048, 771, 691 cm^{-1}; MS (ESI) m/z 373 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{25}H_{25}O_3$ $(M + H)^+$ 373.1798, found 373.1797.

*2-Benzyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ab**).* 320 mg, 93% yield, white solid: mp 143−144 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, J = 7.2 Hz, 2H), 7.53 (dd, J = 7.4, 7.2 Hz, 1H), 7.44 (t, J = 7.2 Hz, 2H), 7.25 (dd, J = 7.4, 7.2 Hz, 2H), 7.20−7.13 (m, 3H), 4.27 (s, 2H), 3.92 (s, 2H), 2.82 (t, J = 6.2 Hz, 2H), 2.41

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(t, J = 6.2 Hz, 2H), 2.21−2.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 195.2, 165.9, 151.7, 137.2, 136.8, 132.8, 128.4, 128.4, 128.3, 128.2, 126.5, 120.3, 111.4, 37.8, 33.4, 32.0, 23.3, 22.4; IR (KBr) ν_{max} = 3062, 3029, 2944, 1671, 1587, 1454, 1343, 1214, 1010, 889, 752 cm^{-1}; MS (ESI) m/z 345 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{23}H_{21}O_3$ (M + H)$^+$ 345.1485, found 345.1483.

2-Benzyl-6-methyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ac**). 347 mg, 97% yield, white solid: mp 138−139 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.7 Hz, 2H), 7.55 (dd, J = 7.7, 6.6 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 7.27 (t, J = 7.7 Hz, 2H), 7.22−7.18 (m, 3H), 4.31 (s, 2H), 3.94 (s, 2H), 2.88 (dd, J = 4.4, 16.4 Hz, 1H), 2.52−2.38 (m, 3H), 2.21 (dd, J = 10.9, 15.4 Hz, 1H), 1.14 (d, J = 5.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 194.9, 165.7, 151.9, 137.2, 136.7, 132.9, 128.5, 128.4, 128.3, 128.2, 126.5, 119.9, 111.3, 46.3, 33.4, 32.0, 31.4, 30.6, 20.9; IR (KBr) ν_{max} = 3029, 2908, 1671, 1588, 1452, 1344, 1215, 1042, 769 cm^{-1}; MS (ESI) m/z 359 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{24}H_{23}O_3$ (M + H)$^+$ 359.1641, found 359.1638.

2-Benzyl-6-isopropyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ad**). 351 mg, 91% yield, white solid: mp 88−89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.2. 1.4 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.3 Hz, 2H), 7.30−7.25 (m, 2H), 7.22−7.18 (m, 3H), 4.31 (s, 2H), 3.93 (s, 2H), 2.85 (dd, J = 17.0, 4.7 Hz, 1H), 2.55 (dd, J = 17.0, 11.1 Hz, 1H), 2.47 (dd, J = 16.2, 3.8 Hz, 1H), 2.24 (dd, J = 16.2, 12.8 Hz, 1H), 2.14−2.05 (m, 1H), 1.71−1.62 (m, 1H), 0.95 (dd, J = 6.7, 2.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 195.2, 166.3, 152.0, 137.2, 136.8, 132.9, 129.2, 128.5, 128.4, 128.3, 126.5, 120.0, 111.2, 42.1, 41.9, 33.4, 32.1, 31.9, 26.9, 19.7, 19.4; IR (KBr) ν_{max} = 3028, 2960, 1692, 1672, 1593, 1451, 1343, 1213, 1049, 753 cm^{-1}; MS (ESI) m/z 387 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{26}H_{27}O_3$ (M + H)$^+$ 387.1954, found 387.1949.

2-Benzyl-3-(2-oxo-2-phenylethyl)-6-phenyl-6,7-dihydrobenzofuran-4(5H)-one (**3ae**). 416 mg, 99% yield, white solid: mp 136−137 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 7.5 Hz, 2H), 7.57 (dd, J = 7.5, 6.0 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.38−7.17 (m, 10H), 4.34 (s, 2H), 3.96 (s, 2H), 3.62−3.49 (m, 1H), 3.16−2.98 (m, 2H), 2.81−2.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 193.8, 165.2, 152.3, 142.5, 137.1, 136.7, 132.9, 128.8, 128.7, 128.5, 128.4, 128.3, 127.0, 126.6, 126.5, 120.2, 111.4, 45.1, 41.2, 33.5, 32.0, 31.1; IR (KBr) ν_{max} = 3028, 2908, 1670, 1588, 1452, 1345, 1218, 1047, 772 cm^{-1}; MS (ESI) m/z 421 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{29}H_{25}O_3$ (M + H)$^+$ 421.1798, found 421.1794.

2-Benzyl-6-(4-methoxyphenyl)-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3af**). 436 mg, 97% yield, white solid: mp 121−123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.2, 1.4 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.9 Hz, 2H), 7.28 (d, J = 7.6 Hz, 2H), 7.23−7.19 (m, 3H), 7.17 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 4.34 (s, 2H), 3.95 (s, 2H), 3.80 (s, 3H), 3.54−3.46 (m, 1H), 3.07 (dd, J = 17.1, 5.0 Hz, 1H), 2.96 (dd, J = 17.2, 11.3 Hz, 1H), 2.73−2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 194.0, 165.3, 158.4, 152.2, 137.1, 136.7, 134.6, 132.9, 128.5, 128.4, 128.4, 128.3, 127.6, 126.5, 120.2, 114.0, 111.4, 55.1, 45.4, 40.4, 33.5, 32.0, 31.4; IR (KBr) ν_{max} = 3028, 2922, 2850, 1671, 1585, 1454, 1343, 1251, 1040, 754 cm^{-1}; MS (ESI) m/z 451 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{30}H_{27}O_4$ (M + H)$^+$ 451.1903, found 451.1895.

2-Benzyl-6-(4-(dimethylamino)phenyl)-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ag**). 458 mg, 99% yield, violet color solid: mp 143−144 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.2, 1.5 Hz, 2H), 7.57 (t, J = 7.6 Hz, 1H), 7.47 (t, J = 6.8 Hz, 2H), 7.32−7.19 (m, 5H), 7.13 (d, J = 8.3 Hz, 2H), 6.71 (d, J = 8.3 Hz, 2H), 4.33 (s, 2H), 3.95 (s, 2H), 3.52−3.39 (m, 1H), 3.07 (dd, J = 17.3, 5.3 Hz, 1H), 2.95 (dd, J = 16.6, 11.3 Hz, 1H), 2.93 (s, 6H), 2.76−2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 194.4, 165.7, 152.1, 149.6, 137.2, 136.7, 132.9, 130.4, 128.5, 128.4, 128.4, 128.3, 127.3, 126.5, 120.1, 112.6, 111.4, 45.6, 40.5, 40.4, 33.5, 32.1, 31.4; IR (KBr) ν_{max} = 3021, 2911, 2851, 1669, 1522, 1451, 1345, 1216, 1047, 772 cm^{-1}; MS (ESI) m/z 464 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{31}H_{30}O_3N$ (M + H)$^+$ 464.2220, found 464.2227.

6-(Benzo[d][1,3]dioxol-4-yl)-2-benzyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ah**). 450 mg, 97% yield, white solid: mp 158−159 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.4, 1.4 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 7.9 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 7.25−7.17 (m, 3H), 6.78−6.68 (m, 3H), 5.95 (s, 2H), 4.33 (s, 2H), 3.95 (s, 2H), 3.51−3.42 (m, 1H), 3.06 (dd, J = 17.1, 5.0 Hz, 1H), 2.94 (dd, J = 17.1, 11.1 Hz, 1H), 2.72−2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 193.8, 165.1, 152.3, 147.8, 146.4, 137.1, 136.7, 136.5, 133.0, 128.6, 128.5, 128.4, 128.3, 126.6, 120.2, 119.7, 111.4, 108.4, 107.0, 101.0, 45.5, 41.0, 33.5, 32.1, 31.5; IR (KBr) ν_{max} = 2918, 2851, 1670, 1586, 1489, 1347, 1219, 1039, 772 cm^{-1}; MS (ESI) m/z 465 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{30}H_{25}O_5$ (M + H)$^+$ 465.1696, found 465.1690.

2-Benzyl-6-(furan-2-yl)-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ai**). 337 mg, 82% yield, white solid: mp 155−157 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.5, 1.4 Hz, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.9 Hz, 2H), 7.34 (d, J = 1.7 Hz, 1H), 7.30−7.19 (m, 5H), 6.30 (dd, J = 3.5, 1.8 Hz, 1H), 6.06 (d, J = 3.5 Hz, 1H), 4.32 (d, J = 13.1 Hz, 2H), 3.94 (s, 2H), 3.67−3.59 (m, 1H), 3.20 (dd, J = 17.2, 5.2 Hz, 1H), 3.02 (dd, J = 17.2, 10.1 Hz, 1H), 2.76 (dd, J = 16.5, 4.3 Hz, 1H), 2.68 (dd, J = 16.6, 11.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 193.2, 164.4, 155.6, 152.4, 141.6, 137.1, 136.7, 132.9, 128.7, 128.6, 128.5, 128.3, 126.6, 120.3, 111.4, 110.1, 104.8, 42.4, 34.4, 33.5, 32.1, 28.5; IR (KBr) ν_{max} = 3025, 2917, 1679, 1589, 1454, 1337, 1211, 1045, 745 cm^{-1}; MS (ESI) m/z 411 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{27}H_{23}O_4$ (M + H)$^+$ 411.1590, found 411.1587.

2-(4-Acetyl-2-benzyl-5-methylfuran-3-yl)-1-phenylethanone (**3aj**). 235 mg, 71% yield, pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.6, 1.7 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.28−7.22 (m, 3H), 7.21−7.17 (m, 2H), 4.10 (s, 2H), 4.02 (s, 2H), 2.57 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.3, 194.8, 158.5, 151.3, 140.1, 137.9, 133.5, 129.7, 128.6, 128.5, 128.3, 126.8, 125.1, 115.9, 33.6, 32.7, 26.4, 21.5; IR (KBr) ν_{max} = 2921, 1619, 1414, 1243, 780, 689 cm^{-1}; MS (ESI) m/z 333 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{22}H_{21}O_3$ (M + H)$^+$ 333.1485, found 333.1482.

2-(4-Benzoyl-2-benzyl-5-phenylfuran-3-yl)-1-phenylethanone (**3ak**). 433 mg, 95% yield, pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.2, 1.3 Hz, 2H), 7.88 (dd, J = 7.2, 1.8 Hz, 2H), 7.75 (dd, J = 7.0, 1.5 Hz, 2H), 7.53−7.16 (m, 12H), 7.14−7.08 (m, 2H), 4.24 (s, 2H), 4.08 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.6, 196.4, 151.5, 137.7, 136.8, 136.6, 133.2, 133.0, 132.6, 131.6, 129.8, 129.7, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 127.7, 127.5, 126.6, 115.9, 33.6, 32.5; IR (KBr) ν_{max} = 2920, 2846, 1687, 1645, 1580, 1448, 1342, 1215, 898, 754, 692 cm^{-1}; MS (ESI) m/z 479 (M + Na)$^+$; HRMS (ESI) m/z calcd for $C_{32}H_{25}O_3$ (M + H)$^+$ 457.1798, found 457.1794.

Ethyl 5-benzyl-2-methyl-4-(2-oxo-2-phenylethyl)furan-3-carboxylate (**3al**). 242 mg, 67% yield, pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.0, 1.5 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.29−7.14 (m, 5H), 4.29 (s, 2H), 4.10 (q, J = 7.2 Hz, 2H), 3.99 (s, 2H), 2.35 (s, 3H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.3, 163.7, 150.3, 143.6, 142.4, 133.1, 129.0, 128.6, 128.3, 128.2, 126.6, 125.3, 115.0, 109.4, 60.1, 34.8, 32.1, 21.4, 13.9; IR (KBr) ν_{max} = 2929, 1678, 1443, 1201, 759, 688 cm^{-1}; MS (ESI) m/z 363 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{23}H_{23}O_4$ (M + H)$^+$ 363.1590, found 363.1596.

Ethyl 5-benzyl-4-(2-oxo-2-phenylethyl)-2-phenylfuran-3-carboxylate (**3am**). 334 mg, 79% yield, pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.9, 1.9 Hz, 2H), 7.88 (dd, J = 6.9, 1.9 Hz, 2H), 7.60−7.53 (m, 1H), 7.51−7.43 (m, 2H), 7.41−7.33 (m, 3H), 7.31−7.18 (m, 5H), 4.32 (s, 2H), 4.08 (q, J = 7.2 Hz, 2H), 4.01 (s, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 164.0, 156.5, 151.2, 137.3, 136.8, 133.0, 131.5, 130.2, 128.9, 128.6, 128.5, 128.4, 128.0, 127.9, 127.7, 126.5, 115.5, 60.2, 34.6, 32.2, 13.8; IR (KBr) ν_{max} = 2921, 2851, 1693, 1489, 1212, 1096, 753, 690 cm^{-1}; MS (ESI) m/z 447 (M + Na)$^+$; HRMS (ESI) m/z calcd for $C_{28}H_{25}O_4$ (M + H)$^+$ 425.1747, found 425.1736.

Ethyl 5-benzyl-4-(2-oxo-2-phenylethyl)-[2,2′-bifuran]-3-carboxylate (**3an**). 314 mg, 76% yield, pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 1.5 Hz, 1H), 8.02 (dd, J = 7.2, 1.5 Hz, 2H),

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7.62−7.54 (m, 1H), 7.52−7.44 (m, 2H), 7.41 (7, J = 1.7 Hz, 1H), 7.32−7.19 (m, 5H), 6.89 (d, J = 1.5 Hz, 1H), 4.30 (s, 2H), 4.10 (q, J = 7.2 Hz, 2H), 3.99 (s, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 163.8, 150.4, 148.2, 144.5, 143.6, 142.4, 137.4, 136.8, 133.1, 128.6, 128.5, 128.4, 128.1, 126.6, 116.7, 115.0, 109.5, 60.2, 34.9, 32.2, 14.0; IR (KBr) ν_{max} = 2922, 2846, 1695, 1448, 1338, 1218, 1098, 772 cm^{-1}; MS (ESI) m/z 437 (M + Na)$^+$; HRMS (ESI) m/z calcd for $C_{26}H_{23}O_5$ (M + H)$^+$ 415.1540, found 415.1536.

*5-Benzyl-4-(2-oxo-2-phenylethyl)-2-phenylfuran-3-carbonitrile (**3ao**).* 335 mg, 89% yield, pale yellow solid: mp 112−123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.1, 1.5 Hz, 2H), 7.93 (dd, J = 7.2, 1.8 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.51−7.37 (m, 6H), 7.29−7.25 (m, 2H), 7.23−7.18 (m, 2H), 4.12 (s, 2H), 4.04 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.7, 158.1, 151.7, 136.2, 135.9, 133.5, 129.7, 128.9, 128.7, 128.6, 128.5, 128.2, 128.0, 126.8, 125.7, 116.0, 114.6, 94.6, 33.6, 32.7; IR (KBr) ν_{max} = 3030, 2922, 2852, 2224, 1681, 1598, 1448, 1337, 1217, 994, 754, 690 cm^{-1}; MS (ESI) m/z 378 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{26}H_{20}O_2N$ (M + H)$^+$ 378.1488, found 378.1493.

*5-Benzyl-4-(2-oxo-2-phenylethyl)-2-(p-tolyl)furan-3-carbonitrile (**3ap**).* 344 mg, 88% yield, pale yellow solid: mp 166−167 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.2, 1.3 Hz, 2H), 7.82 (d, J = 8.3 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.31−7.16 (m, 7H), 4.10 (s, 2H), 4.02 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.7, 158.5, 151.3, 140.0, 136.3, 136.0, 133.5, 129.5, 128.7, 128.6, 128.5, 128.2, 126.8, 125.4, 125.0, 115.8, 114.8, 93.8, 33.6, 32.6, 21.4; IR (KBr) ν_{max} = 3030, 2922, 2854, 2224, 1687, 1598, 1581, 1450, 1336, 1217, 989, 771, 690 cm^{-1}; MS (ESI) m/z 392 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{27}H_{22}O_2N$ (M + H)$^+$ 392.1645, found 392.1644.

*5-Benzyl-2-(4-methoxyphenyl)-4-(2-oxo-2-phenylethyl)furan-3-carbonitrile (**3aq**).* 370 mg, 91% yield, pale yellow solid: mp 134−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.0, 1.5 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H), 7.30−7.17 (m, 5H), 6.95 (d, J = 8.8 Hz, 2H), 4.10 (s, 2H), 4.01 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.8, 160.6, 158.4, 150.8, 136.4, 135.9, 133.5, 128.7, 128.6, 128.5, 128.2, 126.8, 126.7, 120.9, 115.6, 115.0, 114.2, 92.8, 55.3, 33.5, 32.5; IR (KBr) ν_{max} = 2922, 2840, 2222, 1691, 1607, 1503, 1451, 1304, 1257, 989, 772, 690 cm^{-1}; MS (ESI) m/z 408 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{27}H_{22}O_3N$ (M + H)$^+$ 408.1594, found 408.1586.

*5-Benzyl-2-(3-chlorophenyl)-4-(2-oxo-2-phenylethyl)furan-3-carbonitrile (**3ar**).* 353 mg, 86% yield, pale yellow solid: mp 149−151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.2, 1.4 Hz, 2H), 7.88−7.85 (m, 2H), 7.61 (t, J = 7.5 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.40−7.35 (m, 2H), 7.28 (t, J = 7.6 Hz, 2H), 7.23−7.18 (m, 3H), 4.11 (s, 2H), 4.04 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 156.3, 152.4, 135.9, 135.8, 135.0, 133.6, 130.2, 129.7, 129.2, 128.8, 128.7, 128.6, 128.5, 128.2, 126.9, 124.9, 123.1, 116.4, 114.2, 33.5, 32.7; IR (KBr) ν_{max} = 3030, 2922, 2852, 2226, 1691, 1597, 1450, 1335, 1216, 990, 769, 689 cm^{-1}; MS (ESI) m/z 412 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{26}H_{19}ClO_2N$ (M + H)$^+$ 412.1098, found 412.1095.

*Methyl 4-(5-benzyl-3-cyano-4-(2-oxo-2-phenylethyl)furan-2-yl)-benzoate (**3as**).* 343 mg, 79% yield, pale yellow solid: mp 161−163 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, J = 8.6, 1.8 Hz, 2H), 8.00 (dd, J = 8.6, 1.5 Hz, 2H), 7.98 (dd, J = 8.2, 1.4 Hz, 2H), 7.61 (t, J = 7.3 Hz, 1H), 7.50 (t, J = 7.9 Hz, 2H), 7.28 (t, J = 6.9 Hz, 2H), 7.24−7.19 (m, 3H), 4.12 (s, 2H), 4.05 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.4, 166.2, 156.5, 152.9, 135.9, 135.8, 133.6, 131.7, 130.6, 130.1, 128.8, 128.7, 128.5, 128.2, 126.9, 124.7, 116.7, 114.2, 96.5, 52.2, 33.5, 32.7; IR (KBr) ν_{max} = 2952, 2923, 2225, 1722, 1684, 1607, 1433, 1281, 1107, 990, 754, 689 cm^{-1}; MS (ESI) m/z 436 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{28}H_{22}O_4N$ (M + H)$^+$ 436.1543, found 436.1535.

*5-Benzyl-2-(4-fluorophenyl)-4-(2-oxo-2-phenylethyl)furan-3-carbonitrile (**3at**).* 288 mg, 72% yield, pale yellow solid: mp 117−119 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (dd, J = 7.4, 1.3 Hz, 2H), 7.92 (dd, J = 8.9, 5.3 Hz, 2H), 7.61 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 7.30−7.09 (m, 7H), 4.11 (s, 2H), 4.02 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.6, 164.9, 161.6, 157.2, 151.7, 136.2, 135.9, 133.6, 128.7, 128.5, 128.2, 127.3, 124.5, 124.5, 116.3, 115.9, 114.6, 94.4, 33.5, 32.6; IR (KBr) ν_{max} = 3029, 2922, 2853, 2226, 1680, 1598, 1501, 1336, 1233, 837, 752 cm^{-1}; MS (ESI) m/z 396 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{26}H_{19}O_2NF$ (M + H)$^+$ 396.1394, found 396.1389.

*2-(2-Benzyl-5-phenyl-4-(phenylsulfonyl)furan-3-yl)-1-phenylethanone (**3au**).* 359 mg, 73% yield, pale blueish semisolid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 7.2 Hz, 2H), 7.70−7.45 (m, 8H), 7.44−7.31 (m, 5H), 7.30−7.15 (m, 5H), 4.44 (s, 2H), 3.97 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 155.8, 152.2, 145.0, 141.8, 136.6, 133.2, 132.8, 130.4, 129.8, 129.4, 128.7, 128.6, 128.4, 128.2, 127.9, 126.9, 126.8, 123.8, 114.6, 114.8, 34.0, 32.4; IR (KBr) ν_{max} = 2928, 2823, 1669, 1614, 1503, 1421, 1304, 1259, 989, 773, 696 cm^{-1}; MS (ESI) m/z 493 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{31}H_{25}O_4S$ (M + H)$^+$ 493.1468, found 493.1465.

*6,6-Dimethyl-2-(4-methylbenzyl)-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ba**).* 366 mg, 95% yield, white solid: mp 118−119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J = 7.9 Hz, 2H), 7.54 (dd, J = 7.9, 6.9 Hz, 1H), 7.44 (t, J = 7.9 Hz, 2H), 7.07 (s, 4H), 4.28 (s, 2H), 3.89 (s, 2H), 2.67 (s, 2H), 2.30 (s, 2H), 2.28 (s, 3H), 1.15 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 194.6, 164.9, 152.1, 136.6, 135.9, 134.0, 132.7, 129.0, 128.4, 128.3, 128.2, 119.0, 111.0, 52.1, 37.2, 35.0, 33.4, 31.6, 28.4, 20.8; IR (KBr) ν_{max} = 3061, 2958, 2931, 1671, 1589, 1453, 1350, 1216, 1048, 771, 691 cm^{-1}; MS (ESI) m/z 387 (M + H)$^+$. HRMS (ESI) m/z calcd for $C_{26}H_{27}O_3$ (M + H)$^+$ 387.1954, found 387.1949; $C_{25}H_{24}O_3Na$ (M + Na)$^+$ 95.1617, found 395.1614.

*2-(4-Methoxybenzyl)-6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ca**).* 390 mg, 97% yield, white solid: mp 110−111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, J = 8.3 Hz, 2H), 7.58−7.52 (m, 1H), 7.48−7.42 (m, 2H), 7.11 (d, J = 9.0 Hz, 2H), 6.80 (d, J = 9.0 Hz, 2H), 4.29 (s, 2H), 3.87 (s, 2H), 3.75 (s, 3H), 2.68 (s, 2H), 2.31 (s, 2H), 1.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 194.8, 165.0, 158.2, 152.4, 136.7, 132.8, 129.5, 129.2, 128.4, 128.3, 119.1, 113.9, 111.0, 55.1, 52.2, 37.3, 35.1, 33.5, 31.3, 28.5; IR (neat) ν_{max} = 3028, 2926, 2851, 1679, 1595, 1454, 1341, 1251, 1042, 758 cm^{-1}; MS (ESI) m/z 403 (M + H)$^+$. HRMS (ESI) m/z calcd for $C_{26}H_{27}O_4$ (M + H)$^+$ 403.1903, found 403.1900.

*2-(3,5-Dimethoxybenzyl)-6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3da**).* 388 mg, 90% yield, pale yellow solid: mp 124−125 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.2, 1.4 Hz, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.5, Hz, 2H), 7.03 (d, J = 8.8 Hz, 1H), 6.40−6.38 (m, 2H), 4.31 (s, 2H), 3.83 (s, 2H), 3.76 (s, 3H), 3.70 (s, 3H), 2.68 (s, 2H), 2.29 (s, 2H), 1.11 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.5, 194.7, 164.7, 157.8, 152.0, 136.9, 132.7, 130.2, 128.3, 128.1, 117.9, 110.7, 103.8, 98.3, 55.1, 52.2, 37.3, 35.1, 33.5, 28.5, 25.7; IR (KBr) ν_{max} = 2957, 2930, 1671, 1612, 1589, 1454, 1352, 1210, 1042, 772, 691 cm^{-1}; MS (ESI) m/z 433 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{27}H_{29}O_5$ (M + H)$^+$ 433.2009, found 433.1998.

*6,6-Dimethyl-3-(2-oxo-2-phenylethyl)-2-(3-(trifluoromethyl)-benzyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ea**).* 418 mg, 95% yield, white solid: mp 88−89 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.5, 1.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H), 7.48−7.41 (m, 4H), 7.40−7.36 (m, 2H), 4.35 (s, 2H), 3.98 (s, 2H), 2.68 (s, 2H), 2.32 (s, 2H), 1.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 194.8, 165.4, 151.1, 138.2, 136.6, 133.0, 131.9, 128.9, 128.5, 128.4, 125.3, 125.2, 123.5, 123.4, 119.0, 111.9, 52.3, 37.3, 35.2, 33.5, 31.9, 28.5; IR (KBr) ν_{max} = 3064, 2961, 2934, 1692, 1673, 1591, 1451, 1330, 1125, 757, 691 cm^{-1}; MS (ESI) m/z 441 (M + H)$^+$, 463 (M + Na)$^+$; HRMS (ESI) m/z calcd for $C_{26}H_{24}F_3O_3$ (M + H)$^+$ 441.1672, found 441.1679.

*2-(4-Chlorobenzyl)-6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3fa**).* 389 mg, 96% yield, white solid: mp 132−133 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.2, 1.3 Hz, 2H), 7.55 (td, J = 7.2, 2.1 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.22 (d, J = 8.5, 2H), 7.12 (d, J = 8.5, 2H), 4.32 (s, 2H), 3.89 (s, 2H), 2.67 (s, 2H), 2.31 (s, 2H), 1.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6, 194.8, 165.2, 151.6, 136.7, 135.7, 133.0, 132.4, 129.9, 128.6, 128.5, 128.4, 119.1, 111.6, 52.3, 37.4, 35.2, 33.5, 31.5, 28.5; IR (KBr) ν_{max} = 3062, 2959, 2928, 1672, 1590, 1452, 1214, 1048, 754, 691 cm^{-1};

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MS (ESI) m/z 407 $(M + H)^+$, 429 $(M + Na)^+$; HRMS (ESI) m/z calcd for $C_{25}H_{24}ClO_3$ $(M + H)^+$ 407.1408, found 407.1415.

*2-(2-Iodobenzyl)-6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ga**).* 479 mg, 96% yield, white solid: mp 106−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.5, 1.5 Hz, 2H), 7.80 (d, J = 6.8 Hz, 1H), 7.53 (d, J = 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 7.23 (t, J = 8.3 Hz, 1H), 7.15 (dd, J = 7.5, 2.3 Hz, 1H), 6.89 (dd, J = 7.5, 1.5 Hz, 1H), 4.34 (s, 2H), 4.03 (s, 2H), 2.68 (s, 2H), 2.31 (s, 2H), 1.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 194.6, 165.3, 150.6, 139.8, 139.4, 136.8, 132.8, 129.9, 128.5, 128.4, 128.3, 128.2, 119.2, 112.3, 100.2, 52.2, 37.6, 37.4, 35.1, 33.8, 28.6; IR (KBr) ν_{max} = 3059, 2958, 2928, 1694, 1672, 1587, 1453, 1351, 1214, 1048, 753, 690 cm^{-1}; MS (ESI) m/z 499 $(M + H)^+$, 521 $(M + Na)^+$; HRMS (ESI) m/z calcd for $C_{25}H_{24}IO_3$ $(M + H)^+$ 499.0765, found 499.0769.

*6,6-Dimethyl-2-(4-nitrobenzyl)-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ha**).* 358 mg, 86% yield, pale yellow solid: mp 152−153 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.13 (d, J = 8.6 Hz, 2H), 8.03 (d, J = 7.5 Hz, 2H), 7.56 (t, J = 7.1 Hz, 1H), 7.48−7.44 (m, 2H), 7.37 (d, J = 8.6 Hz, 2H), 4.36 (s, 2H), 4.03 (s, 2H), 2.68 (s, 2H), 2.33 (s, 2H), 1.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 194.7, 165.5, 150.3, 146.6, 144.8, 136.4, 133.0, 129.3, 128.4, 128.3, 123.6, 118.9, 112.2, 52.1, 37.2, 35.0, 33.3, 31.8, 28.4; IR (KBr) ν_{max} = 3066, 2959, 2929, 1672, 1593, 1452, 1346, 1048, 755, 690 cm^{-1}; MS (ESI) m/z 418 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{25}H_{24}NO_5$ $(M + H)^+$ 418.1649, found 418.1645.

*6,6-Dimethyl-2-(naphthalen-1-ylmethyl)-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ia**).* 409 mg, 97% yield, pale yellow solid: mp 89−90 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (dd, J = 9.8, 2.7 Hz, 1H), 7.95 (dd, J = 7.5, 1.5 Hz, 2H), 7.81 (dd, J = 7.5, 2.7 Hz, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.55−7.37 (m, 5H), 7.33 (t, J = 8.3 Hz, 1H), 7.22 (d, J = 7.5 Hz, 1H), 4.38 (s, 2H), 4.26 (s, 2H), 2.65 (s, 2H), 2.30 (s, 2H), 1.09 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.5, 194.9, 165.1, 151.4, 136.7, 133.6, 132.9, 132.8, 131.7, 128.6, 128.4, 128.3, 127.4, 126.5, 126.1, 125.6, 125.4, 123.4, 119.3, 111.7, 52.3, 37.3, 35.2, 33.5, 29.7, 28.5; IR (KBr) ν_{max} = 3057, 2958, 2927, 1671, 1591, 1451, 1351, 1216, 1049, 775, 690 cm^{-1}; MS (ESI) m/z 423 $(M + H)^+$, 445 $(M + Na)^+$; HRMS (ESI) m/z calcd for $C_{29}H_{27}O_3$ $(M + H)^+$ 423.1955, found 423.1960.

*6,6-Dimethyl-3-(2-oxo-2-phenylethyl)-2-(thiophen-2-ylmethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ja**).* 362 mg, 96% yield, brown solid: mp 114−115 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.5, 1.5 Hz, 2H), 7.54 (dd, J = 7.5, 2.3 Hz, 1H), 7.45 (t, J = 7.5 Hz, 2H), 7.13 (dd, J = 5.3, 1.5 Hz, 1H), 6.89 (dd, J = 5.3, 3.0 Hz, 1H), 6.83 (d, J = 4.5 Hz, 1H), 4.32 (s, 2H), 4.13 (s, 2H), 2.70 (s, 2H), 2.32 (s, 2H), 1.12 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 194.8, 165.1, 152.2, 139.5, 136.7, 132.9, 128.4, 128.3, 126.8, 125.5, 124.2, 119.1, 111.3, 52.2, 37.3, 35.1, 33.4, 28.5, 26.5; IR (KBr) ν_{max} = 3066, 2959, 2868, 1692, 1672, 1589, 1451, 1351, 1214, 1049, 755, 692 cm^{-1}; MS (ESI) m/z 379 $(M + H)^+$, 401 $(M + Na)^+$; HRMS (ESI) m/z calcd for $C_{23}H_{23}O_3S$ $(M + H)^+$ 379.1362, found 379.1358.

*2-Cinnamyl-6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ka**).* 358 mg, 90% yield, brown solid: mp 124−125 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (t, J = 8.3 Hz, 2H), 7.50−7.45 (m, 1H), 7.41−7.35 (m, 2H), 7.25−7.18 (m, 3H), 7.15−7.11 (d, J = 8.0 Hz, 2H), 6.30 (ddd, J = 15.8, 8.3, 4.2 Hz, 1H), 6.14 (dd, J = 15.8, 1.5 Hz, 1H), 4.29 (d, J = 4.2 Hz, 2H), 3.43 (dd, J = 9.8, 2.6 Hz, 2H), 2.64 (s, 2H), 2.25 (s, 2H), 1.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 194.4, 165.3, 150.6, 139.6, 136.7, 132.9, 132.0, 129.5, 128.4, 128.3, 127.3, 126.1, 124.8, 116.8, 111.4, 52.3, 39.3, 37.4, 35.1, 33.5, 28.5; IR (KBr) ν_{max} = 3061, 2960, 2930, 1671, 1597, 1455, 1352, 1214, 1049, 754, 693 cm^{-1}; MS (ESI) m/z 399 $(M + H)^+$, 421 (M + Na); HRMS (ESI) m/z calcd for $C_{27}H_{27}O_3$ $(M + H)^+$ 399.1955, found 399.1964.

*6,6-Dimethyl-2-nonyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3la**).* 302 mg, 74% yield, pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (dd, J = 7.4, 1.7 Hz, 2H), 7.59−7.41 (m, 3H), 4.28 (s, 2H), 2.70 (s, 2H), 2.52 (t, J = 7.5 Hz, 2H), 2.31 (s, 2H), 1.62−1.51 (m, 2H), 1.34−1.20 (m, 12H), 1.12 (s, 6H), 0.87 (t, J = 3.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.9, 195.0, 164.6, 154.5, 136.9, 132.9, 128.5, 128.4, 119.0, 109.8, 52.4, 37.5, 35.3, 33.7, 31.8, 29.7, 29.5, 29.3, 29.2, 28.7, 28.1, 25.9, 22.6, 14.1; IR (KBr) ν_{max} = 2924, 2854, 1730, 1668, 1457, 1398, 1248, 1081, 761, 696 cm^{-1}; MS (ESI) m/z 409 $(M + H)^+$. HRMS (ESI) m/z calcd for $C_{27}H_{37}O_3$ $(M + H)^+$ 409.2737, found 409.2729.

*2-Benzyl-6,6-dimethyl-3-(2-oxopropyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ma**).* 279 mg, 96% yield, white solid: mp 96−97 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.17 (m, 5H), 3.88 (s, 2H), 3.69 (s, 2H), 2.66 (s, 2H), 2.30 (s, 2H), 2.20 (s, 3H), 1.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.5, 194.8, 165.3, 151.8, 137.2, 128.6, 128.4, 126.6, 124.3, 119.0, 52.2, 38.2, 37.3, 35.2, 32.0, 29.7, 28.6; IR (KBr) ν_{max} = 3057, 2903, 1722, 1671, 1532, 1457, 1214, 1021, 967, 751 cm^{-1}; MS (ESI) m/z 311 $(M + H)^+$. HRMS (ESI) m/z calcd for $C_{20}H_{22}O_3Na$ $(M + Na)^+$ 333.1461, found 333.1460.

*Ethyl 2-(2-benzyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-yl)acetate (**3na**).* 295 mg, 87% yield, colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.23 (m, 3H), 7.22−7.16 (m, 2H), 4.14 (q, J = 7.1 Hz, 2H), 3.92 (s, 2H), 3.64 (s, 2H), 2.66 (s, 2H), 2.31 (s, 2H), 1.25 (t, J = 7.1 Hz, 3H), 1.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 170.8, 165.0, 151.5, 137.2, 128.5, 128.4, 126.6, 119.2, 111.2, 60.7, 52.2, 37.3, 35.2, 31.9, 29.3, 28.5, 14.1; IR (KBr) ν_{max} = 2961, 2928, 1736, 1672, 1586, 1453, 1219, 1030, 772 cm^{-1}; MS (ESI) m/z 341 $(M + H)^+$; 363 (M + Na); HRMS (ESI) m/z calcd for $C_{21}H_{25}O_4$ $(M + H)^+$ 341.1747, found 341.1751.

*Benzyl 2-(2-benzyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-yl)acetate (**3oa**).* 369 mg, 92% yield, white solid: mp 67−68 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.29 (m, 5H), 7.28−7.24 (m, 2H), 7.23−7.19 (m, 1H), 7.18−7.11 (m, 2H), 5.12 (s, 2H), 3.90 (s, 2H), 3.70 (s, 2H), 2.65 (s, 2H), 2.31 (s, 2H), 1.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.5, 170.6, 165.0, 151.6, 137.1, 135.8, 129.6, 128.5, 128.3, 128.2, 128.0, 126.6, 119.2, 111.0, 66.6, 52.2, 37.2, 35.1, 31.9, 29.3, 28.5; IR (KBr) ν_{max} = 3032, 2959, 2923, 1740, 1674, 1589, 1455, 1352, 1216, 1165, 1048, 771 cm^{-1}; MS (ESI) m/z 403 $(M + H)^+$; HRMS (ESI) m/z calcd for $C_{26}H_{27}O_4$ $(M + H)^+$ 403.1903, found 403.1894.

*2-(2-Benzyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-yl)-N,N-diethylacetamide (**3pa**).* 315 mg, 86% yield, colorless liquid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.27 (m, 2H), 7.26−7.18 (m, 3H), 4.02 (s, 2H), 3.70 (s, 2H), 3.43 (q, J = 7.2 Hz, 2H), 3.37 (q, J = 7.0 Hz, 2H), 2.66 (s, 2H), 2.31 (s, 2H), 1.19 (t, J = 7.0 Hz, 3H), 1.12−1.093 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 195.1, 169.3, 165.0, 152.3, 137.7, 128.6, 128.5, 126.4, 119.0, 112.1, 52.5, 42.3, 40.6, 37.4, 35.2, 32.2, 28.6, 28.1, 14.2, 13.0; IR (KBr) ν_{max} = 2961, 2928, 1736, 1622, 1586, 1451, 1270, 1190, 779 cm^{-1}; MS (ESI) m/z 341 $(M + H)^+$; 368 (M + H); HRMS (ESI) m/z calcd for $C_{23}H_{30}NO_3$ $(M + H)^+$ 368.2220, found 368.2222.

*2-(2-Benzyl-6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-3-yl)acetonitrile (**3qa**).* 246 mg, 84% yield, colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44−7.29 (m, 5H), 3.02 (t, J = 7.4 Hz, 2H), 2.77 (s, 2H), 2.66 (t, J = 7.4 Hz, 2H), 2.38 (s, 2H), 1.16 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.1, 165.6, 147.9, 130.5, 129.6, 128.0, 127.6, 121.3, 118.6, 118.4, 52.8, 37.5, 34.8, 28.5, 22.4, 16.3; IR (KBr) ν_{max} = 2959, 2868, 2248, 1678, 1592, 1449, 1218, 1047, 959, 769, 699 cm^{-1}; MS (ESI) m/z 294 $(M + H)^+$. HRMS (ESI) m/z calcd for $C_{19}H_{20}O_2N$ $(M + H)^+$ 294.1488, found 294.1484.

*2-Benzyl-6,6-dimethyl-3-(nitromethyl)-6,7-dihydrobenzofuran-4(5H)-one (**3ra**).* 253 mg, 81% yield, pale yellow solid: mp 134−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.15 (m, 5H), 5.46 (s, 2H), 4.01 (s, 2H), 2.71 (s, 2H), 2.35 (s, 2H), 1.13 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.3, 165.5, 155.4, 130.9, 128.9, 128.6, 127.2, 118.6, 108.1, 68.0, 52.0, 37.1, 32.4, 29.7, 28.6; IR (KBr) ν_{max} = 2958, 2842, 1671, 1562, 1525, 1443, 1229, 1047, 959, 768, 691 cm^{-1}; MS (ESI) m/z 314 $(M + H)^+$. HRMS (ESI) m/z calcd for $C_{18}H_{20}O_4N$ $(M + H)^+$ 314.1386, found 314.1381.

*2-Benzyl-6,6-dimethyl-3-(1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)-6,7-dihydrobenzofuran-4(5H)-one (**3sa**).* 374 mg, 94% yield, white solid: mp 183−184 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (dd, J = 7.8, 1.2 Hz, 1H), 7.46 (td, J = 7.5, 1.4 Hz, 1H), 7.33−7.28 (m, 3H), 7.25−7.20 (m, 4H), 3.96 (s, 2H), 3.77 (d, J = 10.7 Hz, 1H), 3.07 (ddd, J = 12.5, 8.9, 4.3 Hz, 1H), 2.95 (dd, J = 5.6, 4.3 Hz, 1H), 2.71 (d, J = 17.1 Hz, 1H), 2.66 (d, J = 17.3 Hz, 1H), 2.62 (dd, J = 17.3, 4.0 Hz,

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1H), 2.32 (d, J = 16.2 Hz, 1H), 2.23 (d, J = 16.2 Hz, 1H), 2.06−1.99 (m, 1H), 1.13 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.2, 193.5, 165.4, 150.9, 143.4, 137.5, 132.9, 132.6, 128.5, 128.4, 128.3, 127.5, 126.5, 118.4, 117.2, 52.1, 45.2, 37.3, 34.9, 32.2, 30.0, 29.5, 28.7, 28.3; IR (KBr) ν_{max} = 3027, 2957, 2934, 2866, 1669, 1449, 1229, 1041, 715 cm^{-1}; MS (ESI) m/z 341 (M + H)$^+$; 399 (M + H); HRMS (ESI) m/z calcd for $C_{27}H_{27}O_3$ (M + H)$^+$ 399.1955, found 399.1953.

General Procedure for the Synthesis of Substituted Bis-furans (5). To a solution of **4** (0.4 mmol) in 9 mL of acetonitrile was added keto-active methylene **2a** (0.84 mmol) and DBU (0.8 mmol) at room temperature, and the mixture was then heated to 85 °C for 20 h. After the completion of the reaction, the mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel (EtOAc:hexanes) to afford the corresponding bis-furan **5**.

*2,2′-(1,2-Phenylenebis(methylene))bis(6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one) (**5a**).* 215 mg, 81% yield, brown solid: mp 167−168 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (dd, J = 7.1, 1.5 Hz, 4H), 7.53 (t, J = 7.1 Hz, 2H), 7.42 (t, J = 7.9 Hz, 4H), 7.10−7.04 (m, 4H), 4.19 (s, 4H), 3.97 (s, 4H), 2.61 (s, 4H), 2.27 (s, 4H), 1.08 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.5, 194.8, 165.1, 151.2, 136.8, 135.3, 132.9, 129.8, 128.4, 128.3, 127.2, 119.3, 111.8, 52.3, 37.3, 35.2, 33.5, 29.7, 28.6; IR (KBr) ν_{max} = 2950, 2925, 2854, 1671, 1594, 1450, 1351, 1214, 1048, 753, 689 cm^{-1}; MS (ESI) m/z 667.2 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{44}H_{43}O_6$ (M + H)$^+$ 667.3054, found 667.3050.

*2,2′-(1,3-Phenylenebis(methylene))bis(6,6-dimethyl-3-(2-oxo-2-phenylethyl)-6,7-dihydrobenzofuran-4(5H)-one) (**5b**).* 237 mg, 89% yield, brown solid: mp 201−203 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (dd, J = 7.5, 1.9 Hz, 4H), 7.52 (t, J = 7.1 Hz, 2H), 7.42 (t, J = 7.9 Hz, 4H), 7.7 (t, J = 7.5 Hz, 1H), 7.05−7.00 (m, 3H), 4.27 (s, 4H), 3.86 (s, 4H), 2.65 (s, 4H), 2.30 (s, 4H), 1.10 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 194.7, 165.2, 151.9, 137.6, 136.8, 132.9, 128.9, 128.8, 128.4, 128.3, 126.8, 119.2, 111.4, 52.3, 37.4, 35.2, 33.6, 32.0, 28.6; IR (KBr) ν_{max} = 2958, 2924, 2854, 1690, 1670, 1589, 1452, 1351, 1214, 1048, 991, 754, 690 cm^{-1}; MS (ESI) m/z 667.3 (M + H)$^+$, 689.3 (M + Na)$^+$; HRMS (ESI) m/z calcd for $C_{44}H_{43}O_6$ (M + H)$^+$ 667.3054, found 667.3050.

*3,3′-(2-Oxocyclohexane-1,3-diyl)bis(2-benzyl-6,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one) (**5c**).* 224 mg, 93% yield, brown solid: mp 106−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.15 (m, 10H), 4.13−3.88 (m, 6H), 2.64 (s, 4H), 2.49−2.30 (m, 2H), 2.25 (s, 4H), 2.15−2.05 (m, 2H), 2.01−1.90 (m, 2H), 1.09 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 194.6, 165.3, 151.2, 138.1, 128.7, 128.3, 126.2, 118.8, 116.2, 52.6, 47.0, 37.5, 35.2, 33.5, 32.5, 28.7, 28.5, 25.9; IR (KBr) ν_{max} = 3021, 2959, 2914, 2867, 1669, 1465, 1342, 1222, 1064, 715, 698 cm^{-1}; MS (ESI) m/z 603 (M + H)$^+$; HRMS (ESI) m/z calcd for $C_{40}H_{43}O_5$ (M + H)$^+$ 603.3105, found 603.3099.

*3,3′-(4-Oxotetrahydro-2H-thiopyran-3,5-diyl)bis(2-benzyl-6,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one) (**5d**).* 228 mg, 92% yield, brown solid: mp 86−87 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31−7.18 (m, 10H), 3.96 (q, J = 12.7 Hz, 4H), 3.76 (t, J = 12.9 Hz, 2H), 2.80 (d, J = 12.9 Hz, 2H), 2.68−2.60 (m, 5H), 2.32−2.21 (m, 5H) 1.09 (s, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 194.5, 165.4, 151.5, 137.7, 128.6, 128.4, 126.3, 118.5, 115.0, 52.3, 49.6, 37.4, 34.9, 34.5, 32.4, 28.6, 28.4; IR (KBr) ν_{max} = 2957, 2925, 2854, 1716, 1666, 1587, 1450, 1351, 1214, 1048, 971, 763 cm^{-1}; MS (ESI) m/z 621 (M + H)$^+$, 643 (M + Na)$^+$; HRMS (ESI) m/z calcd for $C_{39}H_{41}O_5S$ (M + H)$^+$ 621.2669, found 621.2672.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Trost, B. M. *Science* **1991**, *254*, 1471. (b) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 259.

(2) (a) Bird, C. W.; Cheeseman, G. W. H. *Comprehensive Organic Chemistry*; Pergamon: New York, 1984. (b) Katritzky, A. R. *Advanced Heterocyclic Chemistry*; Academic Press: New York, 1982. (c) Kobayashi, J.; Watanabe, D.; Kawasaki, N.; Tsuda, M. *J. Org. Chem.* **1997**, *62*, 9236. (d) Mulholland, D. A.; Langlois, A.; Randrianarivelojosia, M.; Derat, E.; Nuzillard, J. M. *Phytochem. Anal.* **2006**, *17*, 87. (e) Kate, A. S.; Aubry, I.; Tremblay, m. L.; Kerr, R. G. *J. Nat. Prod.* **2008**, *71*, 1977. (f) Barancelli, D. A.; Mantovani, A. C.; Jesse, C.; Nogueira, C. W.; Zeni, G. *J. Nat. Prod.* **2009**, *72*, 857. (g) Arepalli, S. K.; Sridhar, V.; Rao, J. V.; Kennady, P. K.; Venkateswarlu, Y. *Apoptosis* **2009**, 729. (h) Banerjee, R.; Kumar, H. K. S.; Banerjee, M. *Int. J. Rev. Life Sci.* **2012**, *2*, 7. (i) Wang, S.; Bao, L.; Zhao, F.; Wang, Q.; Li, S.; Ren, J.; Li, L.; Wen, H.; Guo, L.; Liu, H. *J. Agric. Food Chem.* **2013**, *61*, 5122.

(3) (a) D'Souza, D. M.; Mueller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095. (b) Sperry, J. B.; Wright, D. L. *Curr. Opin. Drug Discovery Dev.* **2011**, *8*, 723. (c) Wang, Y.; Luo, Y.-C.; Hu, X.-Q.; Xu, P.-F. *Org. Lett.* **2011**, *13*, 5346. (d) Reichstein, A.; Vortherms, S.; Bannwitz, S.; Tentrop, J.; Prinz, H.; Muller, K. *J. Med. Chem.* **2012**, *55*, 7273.

(4) (a) Gandini, A.; Belgacem, M. N. *Prog. Polym. Sci.* **1997**, *22*, 1203. (b) Wu, C. C.; Hung, W. Y.; Liu, T. L.; Zhang, L. Z.; Luh, T. Y. *J. Appl. Phys.* **2003**, *93*, 5465. (c) Cui, X.; Xu, X.; Wojtas, L.; Kim, M. M.; Zhang, X. P. *J. Am. Chem. Soc.* **2012**, *134*, 19981. (d) Ripaud, E.; Demeter, D.; Rousseau, T.; Boucard-Cetol, E.; Allain, M.; Po, R.; Leriche, P.; Roncali, J. *Dyes Pigm.* **2012**, *95*, 126.

(5) For reviews on furans, see: (a) Wong, H. N. C.; Hou, X. L.; Yeung, K. S.; Huang, H. In *Modern Heterocyclic Chemistry*; Ivarez-Builla, J., Vaquero, J.-J., Barluenga, J., Eds.; Wiley-VCH: Weinheim, 2011. (b) Boto, A.; Ivarez, L. In *Heterocycles in Natural Products Syntheis*; Majumdar, K. C., Chattopdahyay, S. K., Eds.; Wiley-VCH: Weinheim, 2011. (c) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795. (d) Brown, R. C. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 850.

(6) (a) Paal, C. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2756. (b) Knorr, L. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 2863.

(7) From propargylic and homopropargylic alcohols, selected references, see: (a) Nishibayashi, Y.; Yoshikawa, M.; Inada, Y.; Milton, M. D.; Hidai, M.; Uemura, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 2681. (b) Barluenga, J.; Riesgo, L.; Vicente, R.; Lopez, L. A.; Tomas, M. *J. Am. Chem. Soc.* **2008**, *130*, 13528. (c) Cao, H.; Jiang, H.; Yao, W.; Liu, X. *Org. Lett.* **2009**, *11*, 1931. (d) Lenden, P.; Entwistle, D. A.; Willis, M. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 10657. (e) Wang, T.; Chen, X. L.; Chen, L.; Zhan, Z. *Org. Lett.* **2011**, *13*, 3324. (f) Yang, F.; Jin, T.; Bao, M.; Yamamoto, Y. *Chem. Commun.* **2011**, *47*, 4541. (g) Huang, H.; Jiang, H.; Cao, H.; Zhao, J.; Shi, D. *Tetrahedron* **2012**, *68*, 3135. (h) Li, P.; Chai, Z.; Zhao, G.; Zhu, S.-Z. *Synlett* **2008**, 2547. (i) Chen, C.-W.; Luh, T.-Y. *Tetrahedron Lett.* **2009**, *50*, 3263.

(8) From enynol, representative references, see: (a) Bew, S. P.; Knight, D. W. *Chem. Commun.* **1996**, 1007. (b) Gabriele, B.; Salerno, G.; Pascali, F. D.; Costa, M.; Chiusoli, G. P. *J. Org. Chem.* **1999**, *64*, 7693. (c) Gabriele, B.; Salerno, G.; Lauria, E. *J. Org. Chem.* **1999**, *64*, 7687. (d) Du, X.; Chen, H.; Liu, Y. *Chem.—Eur. J.* **2008**, *14*, 9495. (e) Du, X.; Song, F.; Lu, Y.; Chen, H.; Liu, Y. *Tetrahedron* **2009**, *65*, 1839. (f) Zhang, X.; Lu, Z.; Fu, C.; Ma, S. *J. Org. Chem.* **2010**, *75*, 2589. (g) Schneider, C. C.; Caldeora, H.; Gay, B. M.; Back, D. F.; Zeni, G. *Org. Lett.* **2010**, *12*, 936. (h) Xiangwei, D.; Haoyi, C.; Yifeng, C.; Jingjin, C.; Yuanhong, L. *Synlett* **2011**, 1010. (i) Gabriele, B.; Mancuso, R.; Maltese, V.; Veltri, L.; Salerno, G. *J. Org. Chem.* **2012**, *77*, 8657. (j) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.*

2000, *122*, 11553. (k) Hashmi, A. S. K.; Häffner, T.; Rudolph, M.; Rominger, F. *Eur. J. Org. Chem.* **2011**, 667.

(9) From enynediones, see: (a) Vicente, R.; Gonzalez, J.; Riesgo, L.; Gonzalez, J.; Lopez, L. A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8063. (b) Gonzalez, J.; Gonzalez, J.; Perez-Calleja, C.; Lopez, L. A.; Vicente, R. *Angew. Chem., Int. Ed.* **2013**, *52*, 1. (c) Clark, J. S.; Boyer, A.; Aimon, A.; Garcia, P. E.; Lindsay, D. M.; Symington, A. D. F.; Danoy, Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 12128. (d) Cao, H.; Zhan, H.; Cen, J.; Lin, J.; Lin, Y.; Zhu, Q.; Fu, M.; Jiang, H. *Org. Lett.* **2013**, *15*, 1080. (e) Zhan, H.; Lin, X.; Qiu, Y.; Du, Z.; Li, P.; Li, Y.; Cao, H. *Eur. J. Org. Chem.* **2013**, 2284.

(10) From 2-(1-alkynyl)-2-alkene-1-ones, see: (a) Yao, T.; Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2004**, *126*, 11164. (b) Yao, T.; Zhang, X.; Larock, R. C. *J. Org. Chem.* **2005**, *70*, 7679. (c) Patil, N. T.; Wu, H.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 4531. (d) Liu, Y.; Zhou, S. *Org. Lett.* **2005**, *7*, 4609. (e) Oh, C. H.; Reddy, V. R.; Kim, A.; Rhim, C. Y. *Tetrahedron Lett.* **2006**, *47*, 5307. (f) Xueyuan, L.; Zhenliang, P.; Xingzhong, S.; Xinhua, D.; Yongmin, L. *Synlett* **2006**, 1962. (g) Xiao, Y.; Zhang, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1903. (h) Liu, F.; Yu, Y.; Zhang, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 5505. (i) Liu, R.; Zhang, J. *Chem.—Eur. J.* **2009**, *15*, 9303. (j) Xiao, Y.; Zhang, J. *Chem. Commun.* **2009**, *45*, 3594. (k) Xiao, Y.; Zhang, J. *Adv. Synth. Catal.* **2009**, *351*, 617. (l) Liu, F.; Qian, D.; Li, L.; Zhao, X.; Zhang, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 6669. (m) Gao, H.; Zhao, X.; Yu, Y.; Zhang, J. *Chem.—Eur. J.* **2010**, *16*, 456. (n) Li, W.; Zhang, J. *Chem. Commun.* **2010**, *46*, 8839.

(11) From 2-alken-4-yn-1-ones, see: (a) Nakatani, K.; Tanabe, K.; Saito, I. *Tetrahedron Lett.* **1997**, *38*, 1207. (b) Nakatani, K.; Adachi, K.; Tanabe, K.; Saito, I. *J. Am. Chem. Soc.* **1999**, *121*, 8221. (c) Miki, K.; Nishino, F.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 5260. (d) Miki, K.; Yokoi, T.; Nishino, F.; Kato, Y.; Washitake, Y.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2004**, *69*, 1557. (e) Kuroda, H.; Hanaki, E.; Kawakami, M. *Tetrahedron Lett.* **1999**, *40*, 3753. (f) Kuroda, H.; Hanaki, E.; Izawa, H.; Kano, M.; Itahashi, H. *Tetrahedron* **2004**, *60*, 1913. (g) Herndon, J. W.; Wang, H. *J. Org. Chem.* **1998**, *63*, 4564. (h) Casey, C. P.; Strotman, N. A. *J. Org. Chem.* **2005**, *70*, 2576. (i) Hashmi, A. S. K.; Sinha, P. *Adv. Synth. Catal.* **2004**, *346*, 432.

(12) Representative references for other alkyne-based methods, see: (a) Liu, W.; Jiang, H.; Zhang, M.; Qi, C. *J. Org. Chem.* **2010**, *75*, 966. (b) Li, Y.; Wheeler, K. A.; Dembinski, R. *Eur. J. Org. Chem.* **2011**, 2767. (c) Hu, J.; Wei, Y.; Tong, X. *Org. Lett.* **2011**, *13*, 3068. (d) Rodriguez, A.; Moran, W. J. *Tetrahedron Lett.* **2011**, *52*, 2605. (e) Cui, X.; Xu, X.; Wojtas, L.; Kim, M. M.; Zhang, X. P. *J. Am. Chem. Soc.* **2012**, *134*, 19981. (f) Bai, Y.; Tao, W.; Ren, J.; Wang, Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 4112. (g) Dateer, R. B.; Pati, K.; Liu, R. *Chem. Commun.* **2012**, *48*, 7200. (h) Swenson, A. K.; Higgins, K. E.; Brewer, M. G.; Brennessel, W. W.; Coleman, M. G. *Org. Biomol. Chem.* **2012**, *10*, 7483. (i) Cao, H.; Zhan, H.; Wu, J.; Zhong, H.; Lin, Y.; Zhang, H. *Eur. J. Org. Chem.* **2012**, 2318. (j) Li, Y.; Wheeler, K. A.; Dembinski, R. *Org. Biomol. Chem.* **2012**, *10*, 2395. (k) Li, E.; Yao, W.; Xie, X.; Wang, C.; Shao, Y.; Li, Y. *Org. Biomol. Chem.* **2012**, *10*, 2960. (l) Li, J.; Liu, L.; Ding, D.; Sun, J.; Li, Y.; Dong, J. *Org. Lett.* **2013**, *15*, 2883.

(13) Selected references for allene-based methods, see: (a) Hashmi, A. S. K.; Ruppert, T. L.; Knöfel, T.; Bats, J. W. *J. Org. Chem.* **1997**, *62*, 7295. (b) Hashmi, A. S. K.; Schwarz, L.; Choi, J. H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (c) Ma, S.; Zhang, J. *Chem. Commun.* **2000**, 117. (d) Ma, S.; Li, L. *Org. Lett.* **2000**, *2*, 941. (e) Ma, S.; Yu, Z. *Angew. Chem., Int. Ed.* **2002**, *41*, 1775. (f) Ma, S.; Zhang, J.; Lu, L. *Chem.—Eur. J.* **2003**, *9*, 2447. (g) Kim, J. T.; Kelin, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2003**, *42*, 98. (h) Sromek, A. W.; Kelin, A. V.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 2280. (i) Zhou, C. Y.; Chan, P. W. H.; Che, C. M. *Org. Lett.* **2006**, *8*, 325. (j) Dudnik, A. S.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 5195. (k) Dudnik, A. S.; Xia, Y.; Li, Y.; Gevorgyan, V. *J. Am. Chem. Soc.* **2010**, *132*, 7645. (l) Hu, J.; Dong, W.; Wu, X.-Y.; Tong, X. *Org. Lett.* **2012**, *14*, 5530.

(14) Representative references for other methods, see: (a) Xi, L.; Huang, X.; Zhong, F. *Org. Lett.* **2006**, *8*, 5061. (b) Fournier, J.; Arseniyadis, S.; Cossy, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 7562. (c) Huang, X.; Peng, B.; Luparia, M.; Gomes, L. F. R.; Veiros, L. F.; Maulide, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 8886. (d) Kim, H. Y.; Li, J.; Oh, K. *J. Org. Chem.* **2012**, *77*, 11132. (e) Jiang, Y.; Zhong, V.; Khong, Y.; Lourdusamy, E.; Park, C. *Chem. Commun.* **2012**, *48*, 3133. (f) Yin, B.; Zeng, G.; Cai, C.; Ji, F.; Huang, L.; Li, Z.; Jiang, H. *Org. Lett.* **2012**, *14*, 616. (g) Zheng, M.; Huang, L.; Wu, W.; Jiang, H. *Org. Lett.* **2013**, *15*, 1838. (h) Song, C.; Ju, L.; Wang, M.; Liu, P.; Zhang, Y.; Wang, J.; Xu, Z. *Chem.—Eur. J.* **2013**, *19*, 3584. (i) Lian, Y.; Huber, T.; Hesp, K. D.; Bergman, R. G.; Eiiman, J. A. *Angew. Chem., Int. Ed.* **2013**, *52*, 629. (j) Butkevich, A. N.; Meerpoel, L.; Stansfield, I.; Angibaud, P.; Corbu, A.; Cossy, J. *Org. Lett.* **2013**, *15*, 3840. (k) Yang, Y.; Yao, J.; Zhang, Y. *Org. Lett.* **2013**, *15*, 3206. (l) Yoshida, M.; Ohno, S.; Shhishido, K. *Chem.—Eur. J.* **2012**, *18*, 1604. (m) Wang, J.; Zhou, R.; He, Z.-R. *Eur. J. Org. Chem.* **2012**, 6033.

(15) (a) Reddy, C. R.; Valleti, R. R.; Reddy, M. D. *J. Org. Chem.* **2013**, *78*, 6495. (b) Reddy, C. R.; Reddy, M. D.; Srikanth, B. *Org. Biomol. Chem* **2012**, *10*, 4280. (c) Reddy, C. R.; Kumaraswamy, P.; Reddy, M. D. *Org. Biomol. Chem.* **2012**, *10*, 4280. (d) Reddy, C. R.; Reddy, M. D.; Srikanth, B.; Prasad, K. R. *Org. Biomol. Chem.* **2011**, *9*, 6027.

(16) The reaction of **1a** with **2a** using DBU in CH_3CN at room temperature provided the Michael addition intermediate **A** (for structure, see Scheme 4).

(17) (a) Mothe, S. R.; Lauw, S. J. L.; Kothandaraman, P.; Chan, P. W. H. *J. Org. Chem.* **2012**, *77*, 6937. (b) Chatterjee, P. N.; Roy, S. *Tetrahedron* **2011**, *67*, 4569. (c) Reddy, C. R.; Vijaykumar, J.; Gree, R. *Synthesis* **2010**, *21*, 3715. (d) Pan, Y.-M.; Zhao, S.-Y.; Ji, W.-H.; Zhan, Z.-P. *J. Comb. Chem.* **2009**, *11*, 103. (e) Ji, W.-H.; Pan, Y. M.; Zhao, S. Y.; Zhan, Z. P. *Synlett* **2008**, 3046. (f) Cadierno, V.; Diez, J.; Gimeno, J.; Nebra, N. *J. Org. Chem.* **2008**, *73*, 5852. (g) Feng, X.; Tan, Z.; Chen, D.; Shen, Y.; Guo, C.-C.; Xiang, J.; Zhu, C. *Tetrahedron Lett.* **2008**, *49*, 4110. (h) Cadierno, V.; Gimeno, J.; Nebra, N. *Adv. Synth. Catal.* **2007**, *349*, 382. (i) Sanz, R.; Miguel, D.; Martinez, A.; Alvarez-Gutierrez, J. M.; Rodriguez, F. *Org. Lett.* **2007**, *9*, 727. (j) Zhan, Z.; Cai, X.; Wang, S.; Yu, J.; Liu, H.; Cui, Y. *J. Org. Chem.* **2007**, *72*, 9838. (k) Zhan, Z.; Wang, S.; Cai, X.; Liu, H.; Yu, J.; Cui, Y. *Adv. Synth. Catal.* **2007**, *349*, 2097.

(18) Lage, S.; Martínez-Estíbalez, U.; Sotomayor, N.; Lete, E. *Adv. Synth. Catal.* **2009**, *351*, 2460.

(19) (a) Nakhai, A.; Bergman, J. *Tetrahedron* **2009**, *65*, 2298. (b) Galambos, J.; Wagner, G.; Nogradi, K.; Bielik, A.; Molnar, L.; Bobok, A.; Horvath, A.; Kiss, B.; Kolok, S.; Nagy, J.; Kurko, D.; Bakk, M. L.; Vastag, M.; Saghy, K.; Gyertyan, I.; Gal, K.; Greiner, I.; Szombathelyi, Z.; Keseru, G. M.; Domany, G. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4371.