JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b01753 • Publication Date (Web): 21 Sep 2018

Tunable Synthesis of 2-Ene-1,4-diones, 4-Hydroxycyclopent-2-en-1-ones and 2-(Furan-3-yl)acetamides *via* Palladium-Catalyzed Cascade Reactions of Allenols

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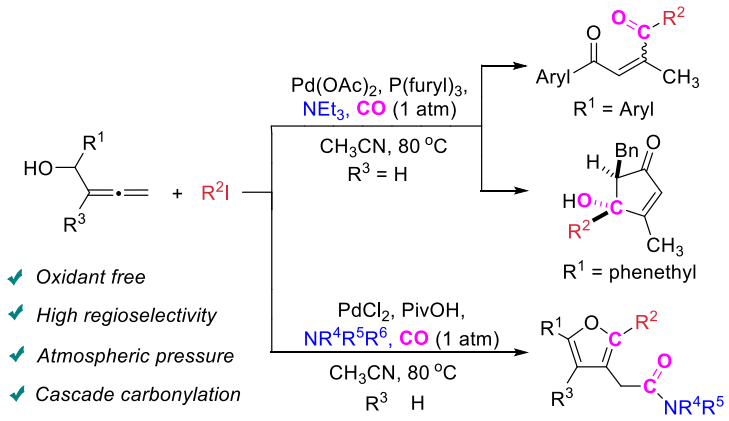
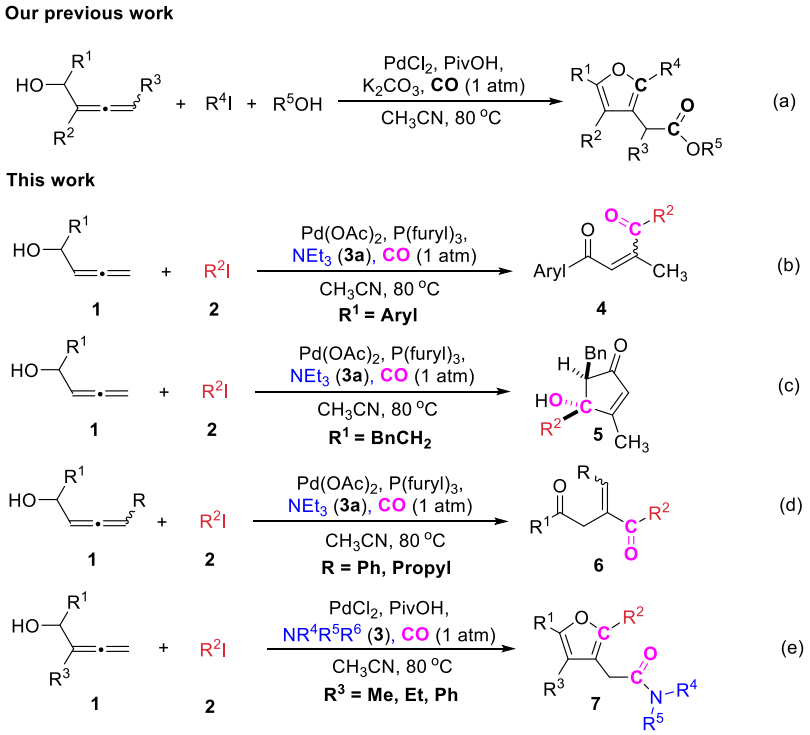


Abstract: An efficient and regio-selective synthesis of 2-ene-1,4-diones, 4-hydroxycyclopent-2-en-1-ones or 2-(furan-3-yl)acetamides is successfully realized through palladium-catalyzed one-pot multi-component reactions of allenols with aryl iodides and carbon monoxide in the presence of tertiary amines. Interestingly, the selectivity is depended on the substitution patterns of the allenol substrates. To be specific, from the reaction of allenols with no substituent attached on the internal position of the allenic moiety, 2-ene-1,4-diones or 4-hydroxycyclopent-2-en-1-ones were formed selectively through carbonylation of aryl iodide followed by acylation of allenol with the *in situ* formed acyl palladium species, β-hydride elimination of the *in situ* formed allyl palladium complex, and further tautomerization or intramolecular Aldol reaction. From the reaction of allenols bearing a substituent at the internal position of the allenic unit, on the other hand, diversely substituted 2-(furan-3-yl)acetamides were formed through a cascade process combining carbonylation of aryl iodide, acylation and cabonylation of allenol followed by intramolecular condensation and amination by tertiary amine featureing with an oxidant-free C–N bond cleavage.

INTRODUCTION

Cascade carbonylation by using CO as a readily available C1 source has become an attractive tool in organic chemistry since it allows rapid generation of structurally diverse carbonyl containing products in a one-pot manner by using simple substrates.[1] Meanwhile, allene derivatives are indispensable intermediates frequently utilized in cascade reactions leading to the formation of advanced organic compounds.[2] In this regard, we have recently reported a novel synthesis of 2-(furan-3-yl)acetate derivatives through palladium-catalyzed and K_2CO_3 promoted one-pot multi-component cascade reactions of allenols with aryl iodides, alcohols and CO (Scheme 1a).[3] As a continuation of our interests in this aspect, we have been trying to prepare 2-(furan-3-yl)acetamide *via* palladium-catalyzed cascade dicarbonylaion of allenols with aryl iodides, tertiary amines, and carbon monoxide. Surprisingly, we found that products 2-ene-1,4-diones, 4-hydroxycyclopent-2-en-1-ones and 2-(furan-3-yl)acetamides can be selectively obtained by controlling the structures of allenols: (i) when allenols without substituents attached on the internal and terminal positions of the allenic moiety were used as substrates, but-2-ene-1,4-diones were afforded as the main products (Scheme 1b). Notably, when phenethyl substituted allenol was used as substrate, 4-hydroxycyclopent-2-en-1-ones were obtained (Scheme 1c). Instead, for allenols with a substituent on the terminal position of allenic moiety, 2-enebutane-1,4-diones were formed selectively (Scheme 1d); (ii) when allenols bearing a substituent attached at the internal position of allenic moiety were used as substrates, dicarbonylation products 2-(furan-3-yl)acetamides could be formed through carbonylation of aryl iodide, acylation and carbonylation of allenols, intramolecular condensation of the α-hydroxylenone intermediate, and amination of the *in situ* formed 2-(furan-3-yl)acetyl palladium complex with tertiary amines *via* oxidant-free C–N bond cleavage (Scheme 1e). In this cascade dicarbonylative reaction, we deduced tertiary amine was not only used as base to

promote the construction of furan structure but also as amine source to participate in aminocarbonylative process *via* C–N bond cleavage without oxidant.



Scheme 1. Diverse Transformations of Allenols

As far as we know, carbonylation between amines and carbon nucleophiles is challenging. The main problem of this transformation is the higher binding affinity of primary or secondary amines to the transition metal.[4] Thus, tertiary amines could be utilized as an alternative amine source to avoid the above mentioned problem.[5] Although, activation of C–N bond of inert tertiary amines as well as utilization of this strategy in cascade process still remains a scientific challenge due to the difficulty of the cleavage of C(sp^3)–N bond[6] and the requirement of oxidants.[5c,7]

In addition, it is well known that furan-carboxamide unit constitutes the core of numerous natural and pharmaceutical compounds.[8] While several efficient and reliable protocols for the preparation of furan-carboxamide derivatives have been developed,[9] most of them usually start from substrates that already have a furan scaffold or suffer from difficult-to-obtain raw materials. On the other hand, 2-ene-1,4-dione and 4-hydroxycyclopent-2-en-1-one derivatives have attracted intensive interest from

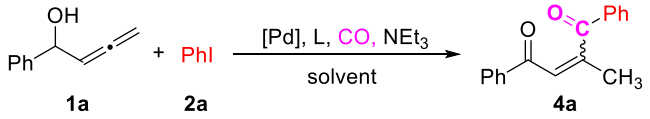
scientists as they are highly valuable intermediates for the synthesis of numerous fine chemicals and pharmaceuticals.[10,11] Therefore, the development of novel and straightforward methods for efficient preparation of 2-ene-1,4-dione, 4-hydroxycyclopent-2-en-1-one and furan-carboxamide scaffolds is an important task in both synthetic and medicinal arena. Based on the above facts, we were interested in a detailed study on the reaction of allenols with aryl iodides, tertiary amines, and carbon monoxide with the aim to develop it into a practical and general protocol for the preparation of 2-ene-1,4-diones, 4-hydroxycyclopent-2-en-1-ones and 2-(furan-3-yl)acetamides.

RESULTS AND DISCUSSION

We started our experiments by using 1-phenylbuta-2,3-dien-1-ol (**1a**), iodobenzene (**2a**) and triethylamine (**3a**) as substrates in a ratio of 1:2:5, in the presence of $PdCl_2$ (10 mol%), and PivOH (40 mol%) under an atmosphere of CO at 80 ºC in CH_3CN for 8 h. From this reaction, product 2-methyl-1,4-diphenylbut-2-ene-1,4-dione (**4a**) was obtained in 51% yield (Table 1, entry 1). In order to improve the yield of **4a**, different palladium salts were tried and $Pd(OAc)_2$ (entry 2) was found to be more effective than $PdCl_2$, $Pd(PPh_3)_2Cl_2$, and $Pd_2(dba)_3$ (entry 1 and entries 3-4). Next, the effect of ligands such as PPh_3, 2-dicyclohexylphosphino -2',4',6'-triisopropylbiphenyl (XPhos), 2-dicyclohexylphosphino-2',4',6'-dimethoxybiphenyl (SPhos), *L*-proline, and $P(2\text{-furyl})_3$ frequently used in palladium catalyzed carbonylation were studied (entries 5-9). It turned out that $P(2\text{-furyl})_3$ is more effective than the other ligands (entry 9 *vs* entry 2 and entries 5-8). In further exploration steps, we tried to decrease or increase the amounts of ligand and catalyst. However, both resulted in lower efficiencies (entries 10-13). We next optimized conditions by using different solvents such as toluene, DCE, 1,4-dioxane, and DMF and found all these attempts did not improve the product yield (entries 14-17). Further changing the reaction temperature to 120 or 40 °C, the reaction gave a relatively lower conversion (entries 18-19). Finally, decreased loading of NEt_3 (3 eq.) (entry 20) and different

bases were tried (entries 21-22). The results showed that NEt_3 (5 eq.) led to the highest yield of **4a** (entry 9 *vs* entries 20-22).

Table 1. Optimization Studies for the Formation of **4a**[a]



1a **2a** **4a**

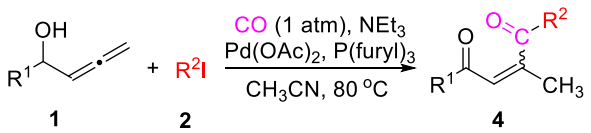
Entry	Catalyst (mol %)	Ligand (mol %)	Solvent	T (°C)	Yield (%) [b]
1	$PdCl_2$ (10)	PivOH (40)	CH_3CN	80	51
2	$Pd(OAc)_2$ (10)	PivOH (40)	CH_3CN	80	60
3	$Pd(PPh_3)_2Cl_2$ (10)	PivOH (40)	CH_3CN	80	Trace
4	$Pd_2(dba)_3$ (5)	PivOH (40)	CH_3CN	80	Trace
5	$Pd(OAc)_2$ (10)	PPh_3 (40)	CH_3CN	80	48
6	$Pd(OAc)_2$ (10)	XPhos(40)	CH_3CN	80	40
7	$Pd(OAc)_2$ (10)	SPhos (40)	CH_3CN	80	30
8	$Pd(OAc)_2$ (10)	L-Proline (40)	CH_3CN	80	47
9	**$Pd(OAc)_2$ (10)**	**P(2-furyl)$_3$ (40)**	**CH_3CN**	**80**	**71**
10	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (20)	CH_3CN	80	35
11	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (80)	CH_3CN	80	51
12	$Pd(OAc)_2$ (20)	P(2-furyl)$_3$ (40)	CH_3CN	80	56
13	$Pd(OAc)_2$ (5)	P(2-furyl)$_3$ (40)	CH_3CN	80	41
14	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	Toluene	80	44
15	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	DCE	80	35
16	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	1,4-Dioxane	80	50
17	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	DMF	80	55
18	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	CH_3CN	120	65
19	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	CH_3CN	40	31
20[c]	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	CH_3CN	80	60
21[d]	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	CH_3CN	80	32
22[e]	$Pd(OAc)_2$ (10)	P(2-furyl)$_3$ (40)	CH_3CN	80	26

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.6 mmol), NEt_3 (1.5 mmol), catalyst (0.03 mmol), ligand (0.12 mmol), solvent (2 mL), CO (1 atm), 8 h. [b] Isolated yields. [c] NEt_3 (0.9 mmol). [d] K_2CO_3 (1.5 mmol). [e] Cs_2CO_3 (1.5 mmol).

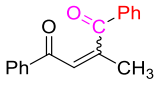
Having established the optimum conditions, a series of allenols (**1**) and iodoaryls (**2**) were tried as substrates and the results are listed in Table 2. Initially, aryl iodides with different substituents attached on the phenyl ring were tested (**4a-4f**). Among them, a sterically

encumbered *o*-methyl iodobenzene seemed reluctant to undergo this reaction, in which **4b** was obtained in 62% yield. Meanwhile, aryl iodide with electron-donating group (EDG) gave the corresponding product (**4d**) in higher yield than that with electron-withdrawing group (EWG) (**4e**). Futhermore, iodothiophene survived the reaction conditions, affording **4g** in moderate yield. Then, we were pleased to find that 1-phenyl substituted allenols with either EDG or EWG on the phenyl ring underwent this cascade process smoothly to give **4h-4j** in moderate to good yields. Notably, thienyl substituted allenol was successfully engaged into this reaction, providing but-2-ene-1,4-dione **4k** with 72% yield.

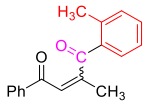
Table 2. Substrate Scope for the Synthesis of **4a-4l**[a,b,c]



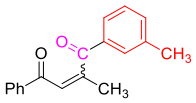
1 2 4



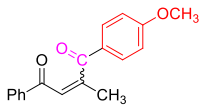
4a, 71%, 5:1



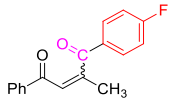
4b, 62%, 2:1



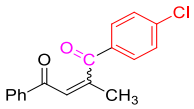
4c, 72%, 6:1



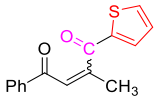
4d, 78%, 4:1



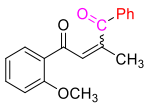
4e, 58%, 7:1



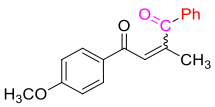
4f, 69%, 5:1



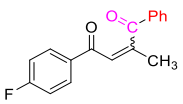
4g, 65%, 6:1



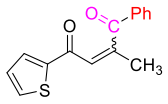
4h, 66%, > 20:1



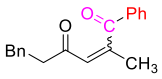
4i, 74%, 8:1



4j, 67%, >20:1



4k, 72%, 6:1

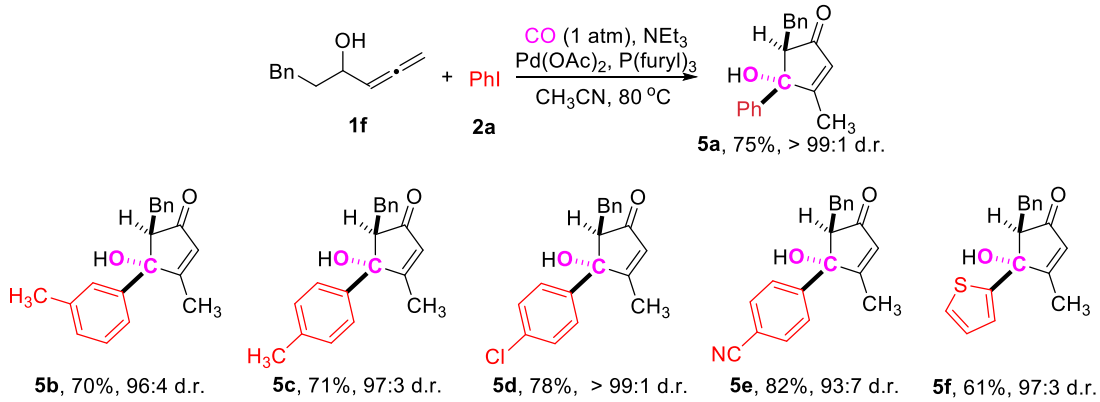


4l, 0%

[a] Reaction conditions: **1** (0.3 mmol), **2** (0.6 mmol), $Pd(OAc)_2$ (0.03 mmol), $P(2\text{-furyl})_3$ (0.12 mmol), Et_3N (1.5 mmol), CH_3CN (2 mL), 80 °C, 8 h, under CO (1 atm). [b] Isolated yield (as a mixture of Z/E isomer). [c] The configuration of double bond in **4** was established based on the corresponding NOE experiments.

When phenethyl-allenol was subjected to this reaction, the desired product **4l** was not obtained. Instead, a cyclic product 5-benzyl-4-hydroxy-3-methyl-4-phenylcyclopent-2-en-1-one (**5a**)[11d] was observed in 75% yield. Considering 4-hydroxycyclopent-2-en-1-one is a key structural unit in numerous compounds displaying significant medicinal activities.[11] Some other aryl iodides

were also tried to explore the generality of this cascade reaction for the formation of 4-hydroxycyclopent-2-en-1-ones. It showed that all of them were suitable substrates to give the corresponding products **5b**-**5f** with good efficiency (Scheme 2).

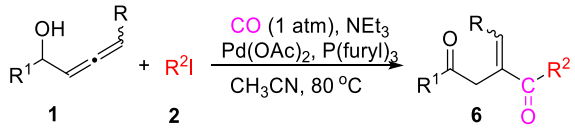


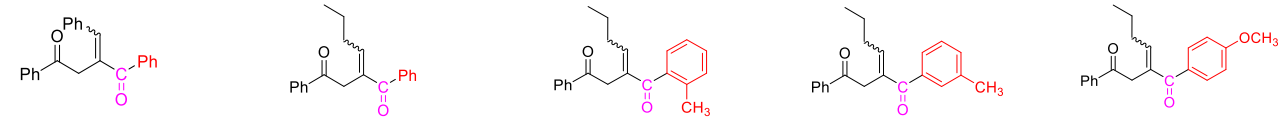
Scheme 2. Synthesis of 4-Hydroxycyclopent-2-en-1-ones (**5**)

Interestingly, when allenols bearing a phenyl or propyl group instead of hydrogen atom at the terminal position of the allenic moiety took part in this reaction, 2-benzylidene-1,4-diphenylbutane-1,4-dione **6a** (82%) and 2-butylidene-1,4-diphenylbutane-1,4-dione **6b** (71%) were obtained in high regioselectivity (Table 3). Next, different aryl iodides (**2**) were tested and it showed that the steric hindrance effect of these substituents had little influence on this reaction (**6c** *vs* **6d**). Aryl iodide with EDG (**6e**) was more favourable than that with EWG (**6f**). Importantly, iodothiophene, thienyl-allenol and alkyl-allenol were also compatible to the reaction conditions, furnishing the corresponding products **6g**, **6h** and **6i** in 65%, 63% and 66% yields, respectively.

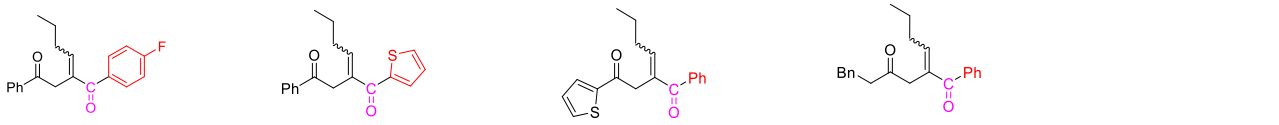
Then, allenol substrate (**1a'**) with substituent attached on the internal position of the allenic moiety was subjected to the standard conditions as shown in Scheme 3. To our surprise, the results showed that dicarbonylation product *N*,*N*-diethyl-2-(4-methyl-2,5-diphenylfuran-3-yl) acetamide (**7a**, 52%) was composed without the formation of 2-ene-1,4-diones (Scheme 3A). After a careful screening of conditions, **7a** was obtained in a maximum yield of 70% by changing $Pd(OAc)_2$ and $P(furyl)_3$ into $PdCl_2$ and PivOH (Scheme 3B).

Table 3. Substrate Scope for the Synthesis of **6** [a,b,c]



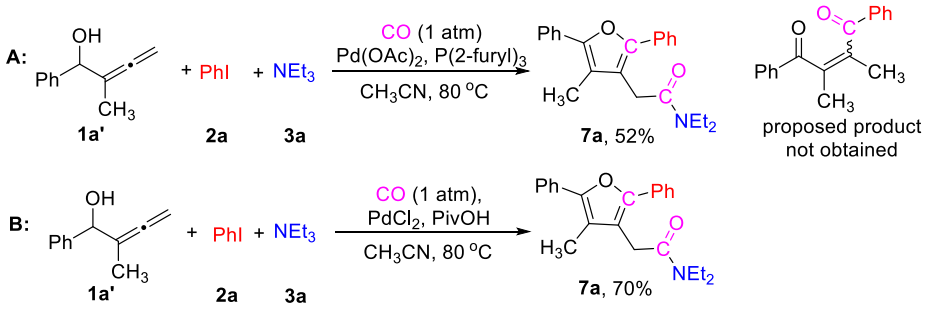


6a, 82%, > 20:1 **6b**, 71%, > 20:1 **6c**, 65%, 4:1 **6d**, 73%, 2:1 **6e**, 78%, 8:1



6f, 60%, 6:1 **6g**, 65%, 9:1 **6h**, 63%, 10:1 **6i**, 66%, 2:1

[a] Reaction conditions: **1** (0.3 mmol), **2** (0.6 mmol), $Pd(OAc)_2$ (0.03 mmol), $P(2\text{-furyl})_3$ (0.12 mmol), Et_3N (1.5 mmol), CH_3CN (2 mL), 80 °C, 8 h, under CO (1 atm). [b] Isolated yield (as a mixture of E/Z isomer). [c] The configuration of double bond in **6** was established based on the corresponding NOE experiments.

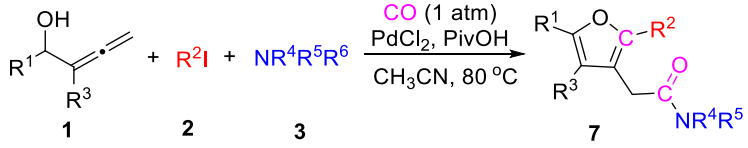


Scheme 3. Formation of 2-(Furan-3-yl)acetamide (**7a**)

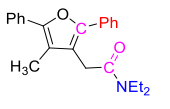
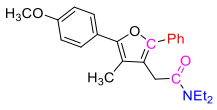
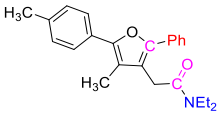
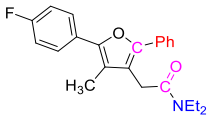
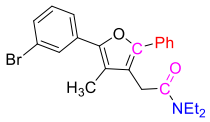
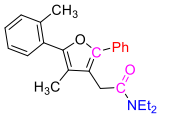
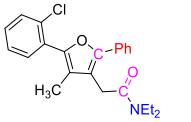
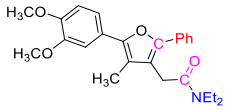
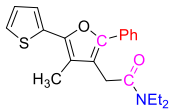
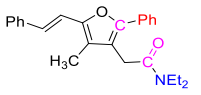
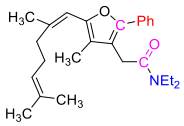
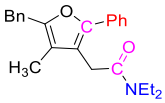
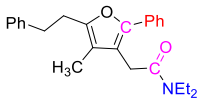
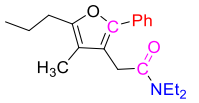
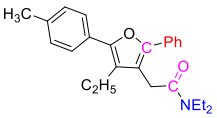
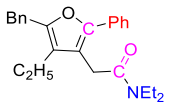
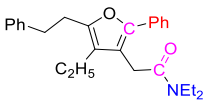
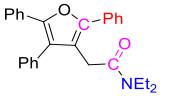
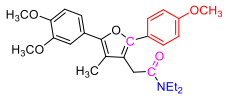
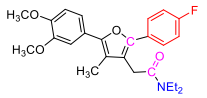
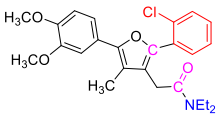
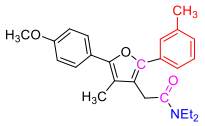
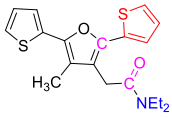
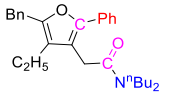
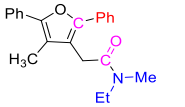
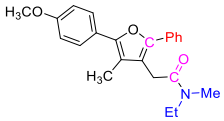
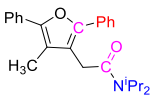
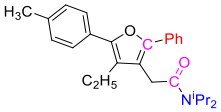
Moreover, we were delighted to find that the fourfold scaled-up reaction afforded a comparable result, wherein the product **7a** was obtained in 68% yield (Table 4). Encouraged by this result, a variety of allenols were used to investigate the scope of this palladium-catalyzed cascade dicarbonylation method leading to the formation of 2-(furan-3-yl)acetamides (**7**). Firstly, various substituents attached on the aromatic ring, including methyl, methoxy, fluoro and even bromo or chloro, which might participate in palladium-catalyzed coupling reactions, survived the reaction conditions, allowing possible subsequent elaboration of the products (**7b**-**7h**), and the electronic nature of these substituents had little influence on this reaction. However, it showed that the obstacle effect with the allenols lead to relatively low yields of **7** (**7f** and **7g**). A

heteroaryl-allenol was also suitable substrate. Thienyl furan (**7i**) could be obtained in a yield as high as 77%.

Table 4. Substrate Scope for the Synthesis of **7** [a,b]



1 2 3 7

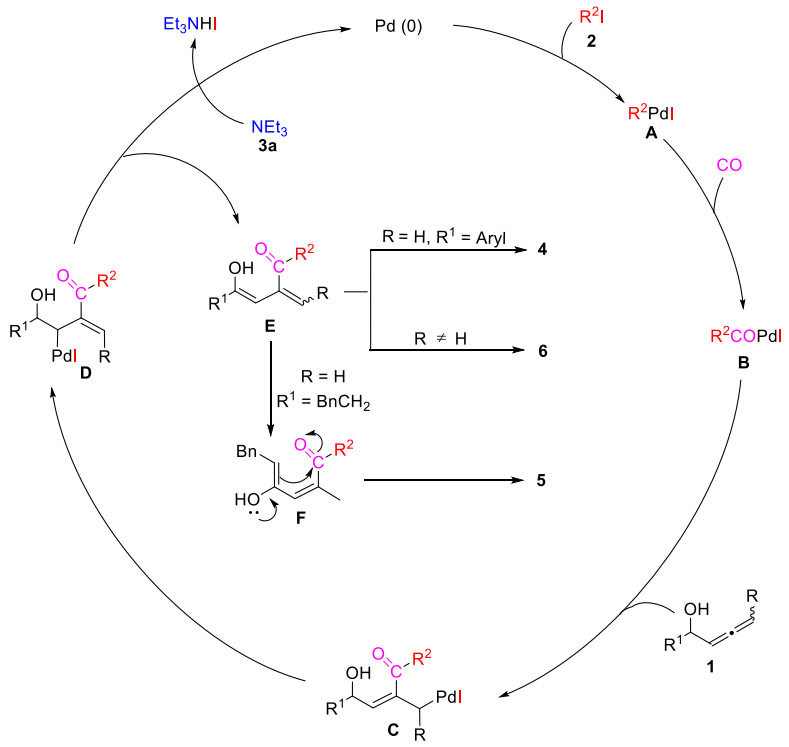
				
7a, 70% (68%)[c]	**7b**, 75%	**7c**, 65%	**7d**, 60%	**7e**, 62%
				
7f, 40%	**7g**, 47%	**7h**, 55%	**7i**, 77%	**7j**, 83%
				
7k, 78%	**7l**, 75%	**7m**, 77%	**7n**, 73%	**7o**, 68%
				
7p, 70%	**7q**, 67%	**7r**, 35%	**7s**, 45%	**7t**, 73%
				
7u, 55%	**7v**, 71%	**7w**, 53%	**7x**, 85% [d]	**7y**, 30% [e,f]
				
7z, 43% [e,g]	**7aa**, 69% [h]	**7bb**, 65% [h]		

[a] Reaction conditions: **1** (0.3 mmol), **2** (0.6 mmol), **3a** (Et_3N, 1.5 mmol), $PdCl_2$ (0.03 mmol), ^{i}PivOH (0.12 mmol), CH_3CN (2 mL), 80 °C, 8 h, under CO (1 atm). [b] Isolated yield. [c] The yield within parentheses was obtained on a 1.2 mmol scale. [d] $^n Bu_3N$ instead of **3a**. [e] Et_2NMe instead of **3a**. [f] **7a** was also obtained in 28% yield at the same time. [g] **7b** was also obtained in 31% yield at the same time. [h] $^i Pr_2NEt$ instead of **3a**.

Apart from aryl-substituted allenols, a cinnamenyl-substituted allenol, a geraniyl-allenol and even alkyl-allenols were well compatible to this reaction affording the differently substituted furyl rings in 73-83% yields (**7j-7n**). Moreover, in addition to methyl group, allenols bearing ethyl or phenyl group on the internal position of the allene moiety could also be converted into

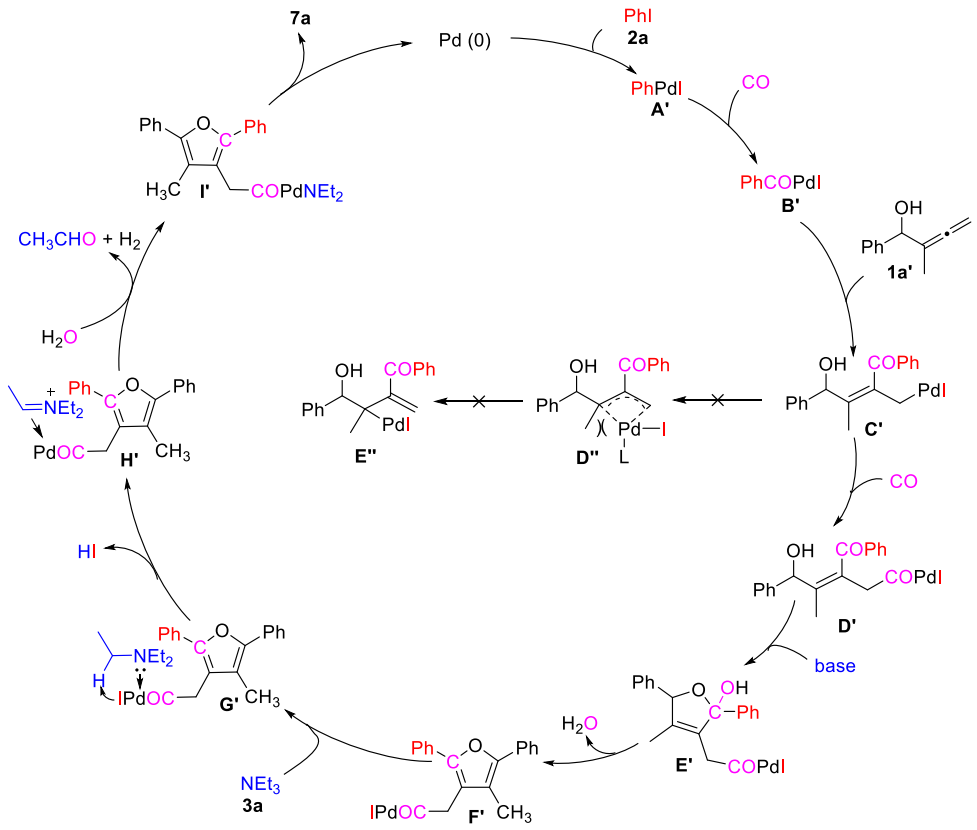
the desired products under the optimized reaction conditions (**7o-7r**). Secondly, the effect of iodoaryls (**2**) was tested by treating different iodoaryls (**2**) with **1** and **3a**. The results showed that the electronic nature of the aryl unit of **2** affected the yield of **7** dramatically (**7s-7v**). In general, **2** with EWG (**7t**) was more favourable than that with EDG (**7s**), and the obstacle of **2** showed some effect on the yield of product (**7u**). Interestingly, starting from 2-iodothiophene, *N,N*-diethyl-2-(4-methyl-2,5-di(thiophen-2-yl)furan-3-yl)acetamide (**7w**) with fluorescence property could be conveniently obtained.[12] Thirdly, to further explore the substrate generality of this reaction, diverse amines (**3**) were treated with different allenols (**1**) and iodobenzene (**2a**). The results showed that symmetric tributylamine with a longer alkyl chain was also compatible with this process and afford the according product (**7x**) in 85% yield. Interestingly, when unsymmetric tertiary amine *N*-ethyl-*N*-methylethanamine was used as substrate, different acetamides (**7a** and **7b** *vs* **7y** and **7z**) were obtained respectively. While, another unsymmetric amine *N*-ethyl-*N*-isobutyl-2-methylpropan-1-amine furnished products **7aa** and **7bb** resulting from the selectively cleaved CH_2–N bonds.

Based on the above observations and previous reports,[3,6c,13,14] plausible pathways accounting for the formation of **4**, **5**, **6** and **7a** are proposed in Scheme 4 and Scheme 5, respectively. Initially, oxidative addition of Pd(0) into **2** forms intermediate **A**, which then undergoes carbonylation to afford an acylpalladium species **B**. In the presence of **1**, alkene coordination and insertion into the Pd–C(O)Ar bond gives an allyl palladium intermediate **C**.[3] Subsequently, 1,3-palladium shift of **C** forms intermediate **D**,[13] which then undergoes β-hydride elimination to afford 4-hydroxy-2-methylene-1,4-diphenylbut-3-en-1-ones **E** and regenerates Pd(0). Then, **E** with hydrogen atoms or substituents on the terminal position of the olefinic moiety, undergoes tautomerization to form **4** or **6**, respectively. Instead, when R^1 is phenethyl group and R is a hydrogen atom, tautomerization of **E** occurs to generate intermediate **F**, which undergoes intramolecular Aldol reaction to give cycle product **5**.



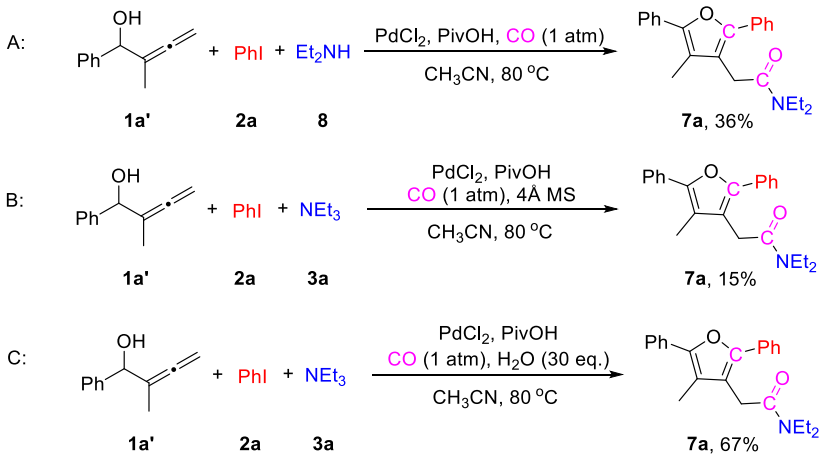
Scheme 4. Plausible Mechanism for the Formation of **4**, **5** and **6**

On the other hand, alkene of **1a'** coordinates and inserts into the Pd–C(O)Ph bond of **B'** which is formed through the carbonylaion of phenylpalladium(II)iodide (**A'**) to give the allyl palladium intermediate **C'**. Due to the steric hindrance influence of methyl group, **C'** is hard to undergo 1,3-palladium shift to form intermediate **D''** and **E''**.[13] The corresponding product 2-ene-1,4-dione will be failed to be obtained. Thus, **C'** undergoes carbonylation to give an acylpalladium complex **D'**.[3] By the action of base, an intramolecular nucleophilic addition occurs with **D'** to afford intermediate **E'**, which undergoes tautomerization and dehydration to form the 2-(furan-3-yl)acetyl palladium complex **F'** and releases water. Then, the palladium of **F'** coordinates with the lone pair of **3a** to form intermediate **G'**. Subsequently, intermediate **H'** is given through the elimination of HI from **G'**. Facilitated by the in situ formed water, **H'** was transformed into **I'** *via* C–N bond cleavage and eliminate acetaldehyde and H_2 as by-products.[6c, 14] Finally, reductive elimination of **I'** affords product **7a** and regenerates Pd(0) (Scheme 5).



Scheme 5. Plausible Mechanism for the Formation of **7a**

To shed some light on the mechanism, control experiments were carried out. At first, the reaction of **1a'** with **2a** and Et_2NH (**8**) was carried out under standard reaction conditions for the formation of 2-(furan-3-yl)acetamides. Under this circumstance, the yield of **7a** decreased to 36% (Scheme 6A), showing that tertiary amine is a more efficient amino source than secondary amine for this reaction. Then, to verify the effect of water in the aminocarbonylative process *via* C–N bond cleavage, 4Å molecule sieves were used to trap the in situ formed water. As a result, **7a** was obtained only in 15% yield (Scheme 6B). In addition, when 30 equiv of H_2O was added in the reaction of **1a'** with **2a, 3a** and CO, **7a** was afforded in 67% yield (Scheme 6C). These results told that water is crucial for aminocarbonylation of allenol **1a'**, and the amount of water which was released from the dehydration of 2,5-dihydrofuran-2-ol intermediate is enough to promote the C–N bond cleavage of tertiary amine **3a**.



Scheme 6. Control Experiments

CONCLUSION

In conclusion, we have established an efficient and regio-selective strategy for the preparation of diversely substituted 2-ene-1,4-diones, 4-hydroxycyclopent-2-en-1-ones and 2-(furan-3-yl)acetamides from palladium-catalyzed and tertiary amines promoted/participated one-pot multi-component reactions of allenols with aryl iodides and carbon monoxide. Notably, in the formation of 2-(furan-3-yl)acetamides, tertiary amine was not only utilized as a base to promote the construction of furan skeleton but also as an amine source to participate in aminocarbonylative process *via* C–N bond cleavage. Compared with previous reports, reactions reported herein have advantages such as high regioselectivity, easily obtainable substrates, good functional group tolerance and step-efficiency. Further exploitation on the detailed mechanism is currently underway in our laboratory.

EXPERIMENTAL SECTION

I. General Experimental Information

Commercial reagents were used without further purification, and the solvents were dried before using. Allenols, with no substituent attached on the internal position of the allenic moiety, were synthesized *via* CuI and diisopropylamine promoted one-pot reactions of 1-substituted prop-2-yn-1-ols with corresponding aldehydes.[15] Allenols, bearing a substituent at the internal position of the allenic unit,

were synthesized through zinc promoted reactions of 1-bromobut-2-yne/1-bromopent-2-yne/ (3-bromoprop-1-yn-1-yl) benzene with the corresponding aldehydes.[3,16] Melting points were recorded with a micro melting point apparatus and uncorrected. The ^{1}H NMR spectra were recorded at 400 MHz or 600 MHz. The ^{13}C NMR spectra were recorded at 100 MHz or 150 MHz. The ^{19}F NMR spectra were recorded at 376 and 565 MHz. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane, and were reported as s (singlet), d (doublet), t (triplet), q (quadruplet), dd (doublet of doublet), td (doublet of triplet), m (multiplet), br s (broad singlet), etc. The coupling constants J were given in Hz. High resolution mass spectra (HRMS) were obtained *via* ESI mode by using a MicrOTOF mass spectrometer. The conversion of starting materials was monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

II. Experimental Procedures and Spectroscopic Data

1. Typical procedure for the preparation of 2-methyl-1,4-diphenylbut-2-ene-1,4-dione (4a)

To a flask containing 1-phenylbuta-2,3-dien-1-ol (**1a**, 44 mg, 0.3 mmol) and iodobenzene (**2a**, 67 μL, 0.6 mmol) in CH_3CN (2 mL) was added $Pd(OAc)_2$ (7 mg, 0.03 mmol), P(2-furyl)$_3$ (28 mg, 0.12 mmol) and Et_3N (**3a**, 208 μL, 1.5 mmol). The mixture was then stirred at 80 ºC under CO atmosphere (1 atm) for 8 h. Upon completion, the reaction was quenched with aqueous NH_4Cl and extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with water and brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum and the crude product was purified by column chromatography on silica-gel to afford **4a-(*Z*)** and **4a-(*E*)** in 59% and 12% yields, respectively. Other 1,4-dione derivatives **4b-4k**, **5a-5f**, and **6a-6i** were prepared in a similar manner.

(*Z*)-2-Methyl-1,4-diphenylbut-2-ene-1,4-dione (4a)[17]

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (44 mg, 59%); ^{1}H NMR (600 MHz, $CDCl_3$) δ:

2.17 (d, J = 1.8 Hz, 3H), 7.077-7.082 (m, 1H), 7.34-7.38 (m, 4H), 7.46 (td, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 2H), 7.82-7.85 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.2, 122.9, 128.4, 128.6, 128.7, 128.8, 133.3, 133.4, 134.5, 136.9, 156.4, 188.1, 199.4. HRMS calcd for $C_{17}H_{14}O_2Na$: 273.0886 $[M+Na]^+$, found: 273.0886.

(*E*)-2-Methyl-1,4-diphenylbut-2-ene-1,4-dione (4a)[17]

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (9 mg, 12%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.28 (d, J = 1.8 Hz, 3H), 7.04 (d, J = 1.2 Hz, 1H), 7.38-7.44 (m, 4H), 7.49-7.54 (m, 2H), 7.80-7.84 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.0, 128.5, 128.7, 128.8, 129.8, 130.5, 133.2, 133.5, 136.2, 137.6, 149.4, 192.1, 198.3. HRMS calcd for $C_{17}H_{14}O_2Na$: 273.0886 $[M+Na]^+$, found: 273.0890.

(*Z*)-2-Methyl-4-phenyl-1-(*o*-tolyl)but-2-ene-1,4-dione (4b)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (33 mg, 41%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.28 (d, J = 1.2 Hz, 3H), 2.73 (s, 3H), 7.06 (q, J = 1.6 Hz, 1H), 7.16 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 7.35 (td, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 1H), 7.40-7.44 (m, 2H), 7.51-7.58 (m, 2H), 7.85-7.88 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 21.8, 22.5, 123.2, 123.52, 123.53, 128.5, 128.6, 130.7, 132.1, 132.3, 133.1, 133.8, 137.1, 140.7, 157.1, 188.7, 200.9. HRMS calcd for $C_{18}H_{16}O_2Na$: 287.1043 $[M+Na]^+$, found: 287.1044.

(*E*)-2-Methyl-4-phenyl-1-(*o*-tolyl)but-2-ene-1,4-dione (4b)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (17 mg, 21%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.26 (d, J = 1.2 Hz, 3H), 2.41 (s, 3H), 7.08 (q, J = 1.6 Hz, 1H), 7.26-7.30 (m, 2H), 7.38-7.48 (m, 4H), 7.56-7.58 (m, 1H), 7.82-7.84 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 14.3, 20.1, 125.4, 128.49, 128.53, 128.9, 130.7, 131.3, 133.7, 134.4, 137.0, 137.3, 137.7, 148.7, 192.7, 200.6. HRMS calcd for $C_{18}H_{16}O_2Na$: 287.1043 $[M+Na]^+$, found: 287.1046.

(*Z*)-2-Methyl-4-phenyl-1-(*m*-tolyl)but-2-ene-1,4-dione (4c)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (49 mg, 62%); ^{1}H NMR (600 MHz, $CDCl_3$) δ:

2.16 (d, J = 1.2 Hz, 3H), 2.29 (s, 3H), 7.07 (d, J = 1.2 Hz, 1H), 7.23 (t, J = 7.8 Hz, 1H), 7.27 (d, J = 7.2 Hz, 1H), 7.35 (t, J = 7.8 Hz, 2H), 7.46 (t, J = 7.8 Hz, 1H), 7.60 (d, J = 7.2 Hz, 1H), 7.69 (s, 1H), 7.83 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 21.4, 22.3, 122.8, 125.8, 128.6, 128.7, 128.8, 133.2, 134.2, 134.5, 137.0, 138.7, 156.5, 188.1, 199.6. HRMS calcd for $C_{18}H_{17}O_2$: 265.1223 $[M+H]^+$, found: 265.1224.

(*E*)-2-Methyl-4-phenyl-1-(*m*-tolyl)but-2-ene-1,4-dione (4c)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (8 mg, 10%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.28 (d, J = 1.6 Hz, 3H), 2.36 (s, 3H), 7.03 (d, J = 1.6 Hz, 1H), 7.31-7.34 (m, 2H), 7.40 (t, J = 7.2 Hz, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.58-7.62 (m, 2H), 7.84 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2H 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 16.0, 21.4, 127.1, 128.46, 128.53, 128.8, 130.2, 130.3, 133.5, 134.0, 136.2, 137.7, 138.6, 149.7, 192.1, 198.5. HRMS calcd for $C_{18}H_{17}O_2$: 265.1223 $[M+H]^+$, found: 265.1220.

(*Z*)-1-(4-Methoxyphenyl)-2-methyl-4-phenylbut-2-ene-1,4-dione (4d)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (52 mg, 62%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.15 (d, J = 1.8 Hz, 3H), 3.74 (s, 3H), 6.83 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 7.03-7.04 (m, 1H), 7.33-7.35 (m, 2H), 7.44-7.46 (m, 1H), 7.79-7.84 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.4, 55.5, 114.1, 122.6, 127.7, 128.6, 128.7, 130.8, 133.2, 137.1, 156.4, 163.8, 188.2, 198.1. HRMS calcd for $C_{18}H_{16}O_3Na$: 303.0992 $[M+Na]^+$, found: 303.0997.

(*E*)-1-(4-Methoxyphenyl)-2-methyl-4-phenylbut-2-ene-1,4-dione (4d)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (13 mg, 16%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.30 (d, J = 1.8 Hz, 3H), 3.81 (s, 3H), 6.90 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 6.98 (d, J = 1.8 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.49 (t, J = 7.2 Hz, 1H), 7.82-7.85 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.5, 55.6, 114.0, 128.3, 128.51, 128.53, 128.8, 132.3, 133.4, 137.9, 150.7, 163.9, 191.9, 196.9. HRMS calcd for $C_{18}H_{16}O_3Na$: 303.0992 $[M+Na]^+$, found: 303.0994.

(*Z*)-1-(4-Fluorophenyl)-2-methyl-4-phenylbut-2-ene-1,4-dione (4e)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (41 mg, 51%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.16 (d, J = 1.2 Hz, 3H), 7.04 (td, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 7.08 (d, J = 1.2 Hz, 1H), 7.35-7.38 (m, 2H), 7.46-7.49 (m, 1H), 7.83-7.87 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.1, 116.0 (d, $^{2}J_{C\text{-}F}$ = 21.9 Hz), 123.0, 128.6, 128.7, 131.0 (d, $^{3}J_{C\text{-}F}$ = 9.8 Hz), 131.1, 133.4, 136.8, 155.9, 165.9 (d, $^{1}J_{C\text{-}F}$ = 252.8 Hz), 188.1, 197.9. ^{19}F NMR (565 MHz, $CDCl_3$) δ: -104.8. HRMS calcd for $C_{17}H_{13}FO_2Na$: 291.0792 $[M+Na]^+$, found: 291.0796.

(*E*)-1-(4-Fluorophenyl)-2-methyl-4-phenylbut-2-ene-1,4-dione (4e)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (6 mg, 7%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.28 (d, J = 1.2 Hz, 3H), 7.00 (d, J = 1.8 Hz, 1H), 7.11 (t, J = 8.4 Hz, 2H), 7.41 (t, J = 7.8 Hz, 2H), 7.51 (t, J = 7.8 Hz, 1H), 7.82-7.86 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.1, 115.9 (d, $^{2}J_{C\text{-}F}$ = 21.9 Hz), 128.5, 128.9, 130.0, 132.4 (d, $^{3}J_{C\text{-}F}$ = 8.7 Hz), 132.5, 133.6, 137.6, 149.4, 165.9 (d, $^{1}J_{C\text{-}F}$ = 239.6 Hz), 191.9, 196.7. ^{19}F NMR (565 MHz, $CDCl_3$) δ: -104.4. HRMS calcd for $C_{17}H_{13}FO_2Na$: 291.0792 $[M+Na]^+$, found: 291.0802.

(*Z*)-1-(4-Chlorophenyl)-2-methyl-4-phenylbut-2-ene-1,4-dione (4f)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (49 mg, 58%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.16 (d, J = 1.8 Hz, 3H), 7.09 (q, J = 1.8 Hz, 1H), 7.33-7.38 (m, 4H), 7.48 (t, J = 7.2 Hz, 1H), 7.76-7.78 (m, 2H), 7.82-7.84 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.0, 123.1, 128.6, 128.7, 129.2, 129.7, 132.9, 133.4, 136.7, 139.7, 155.8, 188.1, 198.2. HRMS calcd for $C_{17}H_{13}ClO_2Na$: 307.0496 $[M+Na]^+$, found: 307.0494.

(*E*)-1-(4-Chlorophenyl)-2-methyl-4-phenylbut-2-ene-1,4-dione (4f)

Eluent: ethyl acetate/petroleum ether (1:20); yellow solid (9 mg, 11%), mp 94-95 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.27 (d, J = 1.2 Hz, 3H), 7.01 (d, J = 1.2 Hz, 1H), 7.39-7.42 (m, 4H), 7.51 (t, J = 7.2 Hz,

1H), 7.75 (d, J = 8.4 Hz, 2H), 7.82 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.0, 128.5, 128.9, 129.0, 130.6, 131.2, 133.7, 134.5, 137.5, 139.7, 149.0, 191.9, 197.0. HRMS calcd for $C_{17}H_{13}ClO_2Na$: 307.0496 $[M+Na]^+$, found: 307.0510.

(*Z*)-2-Methyl-4-phenyl-1-(thiophen-2-yl)but-2-ene-1,4-dione (4g)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (43 mg, 56%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.20 (d, J = 1.6 Hz, 3H), 6.98-6.99 (m, 1H), 7.02 (d, J = 1.2 Hz, 1H), 7.37 (t, J = 7.6 Hz, 2H), 7.47-7.48 (m, 2H), 7.55 (dd, J_1 = 4.8 Hz, J_2 = 1.2 Hz, 1H), 7.83 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.3, 123.4, 128.2, 128.6, 128.7, 132.7, 133.3, 134.1, 137.1, 142.1, 154.7, 188.3, 191.5. HRMS calcd for $C_{15}H_{12}O_2SNa$: 279.0450 $[M+Na]^+$, found: 279.0462.

(*E*)-2-Methyl-4-phenyl-1-(thiophen-2-yl)but-2-ene-1,4-dione (4g)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (7 mg, 9%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.37 (d, J = 1.2 Hz, 3H), 7.17-7.20 (m, 1H), 7.26-7.28 (m, 1H), 7.49 (t, J = 8.0 Hz, 2H), 7.60 (t, J = 7.6 Hz, 1H), 7.76-7.77 (m, 2H), 7.95 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.2, 128.3, 128.5, 128.6, 128.9, 133.6, 134.7, 135.3, 137.7, 142.4, 149.8, 189.9, 191.8. HRMS calcd for $C_{15}H_{12}O_2SNa$: 279.0450 $[M+Na]^+$, found: 279.0450.

(*Z*)-4-(2-Methoxyphenyl)-2-methyl-1-phenylbut-2-ene-1,4-dione (4h)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (55 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.02 (s, 3H), 3.94 (s, 3H), 6.94-6.96 (m, 2H), 7.12 (s, 1H), 7.45 (t, J = 7.6 Hz, 3H), 7.53 (d, J = 7.6 Hz, 2H), 7.96 (d, J = 7.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.0, 55.7, 111.5, 120.8, 127.9, 128.0, 128.5, 128.7, 131.2, 133.2, 133.9, 134.6, 153.0, 158.7, 190.0, 199.7. HRMS calcd for $C_{18}H_{16}O_3Na$: 303.0992 $[M+Na]^+$, found: 303.0992.

(*Z*)-4-(4-Methoxyphenyl)-2-methyl-1-phenylbut-2-ene-1,4-dione (4i)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (55 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ:

2.23 (d, J = 1.2 Hz, 3H), 3.84 (s, 3H), 6.90 (d, J = 8.8 Hz, 2H), 7.13 (d, J = 1.2 Hz, 1H), 7.44 (t, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.90-7.93 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 22.1, 55.5, 113.9, 122.9, 128.4, 128.7, 129.9, 131.0, 133.2, 134.6, 155.4, 163.7, 186.5, 199.6. HRMS calcd for $C_{18}H_{16}O_3Na$: 303.0992 $[M+Na]^+$, found: 303.0992.

(*E*)-4-(4-Methoxyphenyl)-2-methyl-1-phenylbut-2-ene-1,4-dione (4i)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (7 mg, 8%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.24 (d, J = 1.6 Hz, 3H), 3.80 (s, 3H), 6.86 (dd, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 2H), 7.00 (d, J = 1.6 Hz, 1H), 7.43 (t, J = 7.2 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.79-7.83 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 15.8, 55.6, 114.0, 128.6, 129.8, 130.6, 131.0, 131.5, 133.0, 136.4, 148.0, 164.0, 190.7, 198.4. HRMS calcd for $C_{18}H_{16}O_3Na$: 303.0992 $[M+Na]^+$, found: 303.0993.

(*Z*)-4-(4-Fluorophenyl)-2-methyl-1-phenylbut-2-ene-1,4-dione (4j)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (54 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.17 (d, J = 1.2 Hz, 3H), 7.01-7.05 (m, 3H), 7.36-7.39 (m, 2H), 7.46-7.50 (m, 1H), 7.82-7.88 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.3, 115.9 (d, $^2J_{C\text{-}F}$ = 21.8 Hz), 122.5, 128.4, 128.9, 131.3 (d, $^3J_{C\text{-}F}$ = 8.7 Hz), 133.3 (d, $^4J_{C\text{-}F}$ = 2.3 Hz), 133.5, 134.4, 156.8, 165.9 (d, $^1J_{C\text{-}F}$ = 253.8 Hz), 186.6, 199.4. ^{19}F NMR (565 MHz, $CDCl_3$) δ: -104.6. HRMS calcd for $C_{17}H_{13}FO_2Na$: 291.0792 $[M+Na]^+$, found: 291.0799.

(*Z*)-2-Methyl-1-phenyl-4-(thiophen-2-yl)but-2-ene-1,4-dione (4k)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (48 mg, 62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.23 (d, J = 1.6 Hz, 3H), 6.98 (q, J = 1.6 Hz, 1H), 7.12-7.14 (m, 1H), 7.43-7.47 (m, 2H), 7.52-7.56 (m, 1H), 7.63 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1H), 7.77 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.90-7.93 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.1, 122.9, 128.4, 128.5, 128.8, 132.5, 133.4, 134.5, 134.6, 144.3, 156.1, 180.4, 199.1. HRMS calcd for $C_{15}H_{12}O_2SNa$: 279.0450 $[M+Na]^+$, found: 279.0459.

(*E*)-2-Methyl-1-phenyl-4-(thiophen-2-yl)but-2-ene-1,4-dione (4k)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (8 mg, 10%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.44 (d, J = 1.6 Hz, 3H), 7.04 (q, J = 1.6 Hz, 1H), 7.11-7.13 (m, 1H), 7.49-7.53 (m, 2H), 7.61-7.64 (m, 2H), 7.68 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1H), 7.86-7.88 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.1, 128.4, 128.67, 128.72, 129.8, 132.4, 133.3, 134.7, 136.0, 145.7, 150.6, 183.6, 198.2. HRMS calcd for $C_{15}H_{12}O_2SNa$: 279.0450 $[M+Na]^+$, found: 279.0461.

(4*R, 5*R**)-5-Benzyl-4-hydroxy-3-methyl-4-phenylcyclopent-2-en-1-one (5a)**[11d]

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (63 mg, 75%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.86 (s, 3H), 2.20-2.23 (m, 2H), 3.12-3.17 (m, 2H), 6.14 (s, 1H), 6.76 (d, J = 7.2 Hz, 2H), 7.12-7.15 (m, 5H), 7.30-7.34 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.6, 31.4, 62.9, 85.2, 125.8, 126.2, 127.7, 128.30, 128.34, 128.7, 129.3, 139.3, 139.4, 176.7, 204.9. HRMS calcd for $C_{19}H_{17}O_2$: 277.1234 $[M-H]^-$, found: 277.1234.

(4*R, 5*R**)-5-Benzyl-4-hydroxy-3-methyl-4-(*m*-tolyl)cyclopent-2-en-1-one (5b)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (61 mg, 70%);^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.87 (d, J = 1.2 Hz, 3H), 2.14-2.24 (m, 2H), 2.30 (s, 3H), 3.10-3.16 (m, 2H), 6.14 (d, J = 1.6 Hz, 1H), 6.16-6.85 (m, 3H), 7.10-7.26 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.7, 21.6, 31.5, 62.7, 85.3, 122.9, 126.1, 128.2, 128.4, 128.8, 129.4, 139.2, 139.3, 176.7, 205.1. HRMS calcd for $C_{20}H_{19}O_2$: 291.1391 $[M-H]^-$, found: 291.1393.

(4*R, 5*R**)-5-Benzyl-4-hydroxy-3-methyl-4-(*p*-tolyl)cyclopent-2-en-1-one (5c)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (62 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.85 (d, J = 1.2 Hz, 3H), 2.18-2.24 (m, 1H), 2.36 (s, 3H), 2.46 (br s, 1H), 3.05-3.13 (m, 2H), 6.10 (d, J = 1.2 Hz, 1H), 6.80-6.95 (m, 3H), 7.11-7.25 (m, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.6, 21.1, 31.4, 62.9, 85.2, 125.7, 126.1, 128.2, 128.8, 129.0, 129.1, 136.4, 137.4, 139.6, 177.0, 205.2. HRMS calcd for

$C_{20}H_{19}O_2$: 291.1391 $[M-H]^-$, found: 291.1393.

(4*R, 5*R**)-5-Benzyl-4-(4-chlorophenyl)-4-hydroxy-3-methylcyclopent-2-en-1-one (5d)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (73 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.86 (s, 3H), 2.15-2.20 (m, 1H), 2.33 (br s, 1H), 3.13-3.16 (m, 2H), 6.14 (s, 1H), 6.79 (d, J = 7.2 Hz, 2H), 7.03-7.17 (m, 5H), 7.29 (d, J = 7.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.6, 31.4, 62.7, 84.9, 126.3, 127.4, 128.4, 128.5, 128.6, 129.5, 133.7, 138.1, 139.0, 176.4, 204.6. HRMS calcd for $C_{19}H_{16}ClO_2$: 311.0844 $[M-H]^-$, found: 311.0849.

(4*R, 5*R**)-4-(5-Benzyl-1-hydroxy-2-methyl-4-oxocyclopent-2-en-1-yl)benzonitrile (5e)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (75 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.85 (q, J = 1.2 Hz, 3H), 2.03 (br s, 1H), 2.07-2.14 (m, 1H), 3.13-3.23 (m, 2H), 6.20 (d, J = 1.2 Hz, 1H), 6.74-6.76 (m, 2H), 7.13-7.16 (m, 5H), 7.59 (dd, J_1 = 7.8 Hz, J_2 = 1.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.7, 31.5, 62.4, 85.0, 111.6, 118.5, 126.4, 128.4, 128.5, 130.2, 138.5, 145.1, 176.1, 204.4. HRMS calcd for $C_{20}H_{16}NO_2$: 302.1187 $[M-H]^-$, found: 302.1188.

(4*R, 5*R**)-5-Benzyl-4-hydroxy-3-methyl-4-(thiophen-2-yl)cyclopent-2-en-1-one (5f)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (52 mg, 61%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.91 (d, J = 1.2 Hz, 3H), 2.29-2.35 (m, 1H), 2.69 (br s, 1H), 3.04-3.12 (m, 2H), 5.97 (d, J = 1.2 Hz, 1H), 6.55 (dd, J_1 = 3.6 Hz, J_2 = 1.2 Hz, 1H), 6.88-6.93 (m, 3H), 7.07-7.18 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 12.5, 30.3, 61.5, 83.4, 123.5, 124.2, 125.2, 126.4, 127.4, 127.6, 127.7, 138.5, 144.2, 175.4, 203.0. HRMS calcd for $C_{17}H_{15}O_2S$: 283.0798 $[M-H]^-$, found: 283.0787.

2-Benzylidene-1,4-diphenylbutane-1,4-dione (6a)[18]

Eluent: ethyl acetate/petroleum ether (1:20); yellow solid (80 mg, 82%), mp 87-89 °C (lit.[17] 89-90 °C);^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.49 (s, 2H), 7.28-7.38 (m, 5H), 7.44 (s, 1H), 7.51 (t, J = 7.6 Hz, 4H), 7.59 (t, J = 8.4 Hz, 2H), 7.97 (d, J = 7.2 Hz, 2H), 8.05 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$)

δ: 38.6, 128.2, 128.3, 128.7, 128.8, 130.0, 132.0, 133.3, 135.3, 136.1, 136.7, 138.2, 143.9, 197.7, 198.6. HRMS calcd for $C_{23}H_{18}O_2Na$: 349.1199 $[M+Na]^+$, found: 349.1198.

2-Butylidene-1,4-diphenylbutane-1,4-dione (6b)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (62 mg, 71%); ^1H NMR (600 MHz, $CDCl_3$) δ: 0.86 (t, *J* = 7.2 Hz, 3H), 1.39-1.43 (m, 2H), 2.15-2.19 (m, 2H), 4.16 (s, 2H), 6.43 (t, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.70 (d, *J* = 7.2 Hz, 2H), 7.96 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.9, 22.0, 31.4, 36.9, 128.1, 128.3, 128.7, 129.7, 131.6, 133.2, 135.3, 136.8, 138.5, 148.5, 197.0, 198.2. HRMS calcd for $C_{20}H_{20}O_2Na$: 315.1356 $[M+Na]^+$, found: 315.1356.

(*E*)-2-Butylidene-4-phenyl-1-(*o*-tolyl)butane-1,4-dione (6c)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (48 mg, 52%); ^1H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 7.2 Hz, 3H), 1.39-1.45 (m, 2H), 2.17-2.22 (m, 2H), 2.33 (s, 3H), 4.19 (s, 2H), 6.49 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 2H), 7.29-7.33 (m, 2H), 7.49 (t, *J* = 8.0 Hz, 2H), 7.56-7.60 (m, 1H), 8.05-8.07 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.9, 19.6, 21.7, 31.7, 35.7, 125.0, 128.1, 128.3, 128.6, 129.5, 130.6, 133.2, 136.1, 136.7, 136.9, 139.2, 151.9, 196.9, 199.8. HRMS calcd for $C_{21}H_{22}O_2Na$: 329.1512 $[M+Na]^+$, found: 329.1508.

(*Z*)-2-Butylidene-4-phenyl-1-(*o*-tolyl)butane-1,4-dione (6c)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (12 mg, 13%); ^1H NMR (600 MHz, $CDCl_3$) δ: 0.72 (t, *J* = 7.2 Hz, 3H), 1.26-1.29 (m, 2H), 1.76-1.80 (m, 2H), 2.45 (s, 3H), 4.13 (s, 2H), 6.02 (t, *J* = 7.8 Hz, 1H), 7.23-7.26 (m, 2H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.6, 20.3, 22.3, 31.8, 45.1, 125.7, 128.3, 128.6, 130.1, 130.9, 131.3, 133.2, 135.1, 136.6, 137.3, 139.6, 142.6, 198.0, 199.8. HRMS calcd for $C_{21}H_{22}O_2Na$: 329.1512 $[M+Na]^+$, found: 329.1509.

2-Butylidene-4-phenyl-1-(*m*-tolyl)butane-1,4-dione (6d)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (67 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: (**major**) 0.93 (t, *J* = 7.2 Hz, 3H), 1.45-1.51 (m, 2H), 2.21-2.27 (m, 2H), 2.41 (s, 3H), 4.16 (s, 2H), 6.50 (t, *J* = 7.6 Hz, 1H), 7.31-7.36 (m, 2H), 7.42-7.50 (m, 2H), 7.53-7.59 (m, 2H), 7.81-7.83 (m, 1H), 8.03 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2H). (**minor**) 0.75 (t, *J* = 7.2 Hz, 3H), 1.28-1.34 (m, 2H), 1.80-1.86 (m, 2H), 2.40 (s, 3H), 4.15 (s, 2H), 5.90 (t, *J* = 7.6 Hz, 1H), 7.31-7.36 (m, 2H), 7.42-7.50 (m, 2H), 7.53-7.59 (m, 3H), 7.95-7.97 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: (**mixture**) 13.6, 13.9, 21.36, 21.37, 22.0, 22.3, 31.4, 32.3, 36.9, 45.8, 126.9, 127.0, 127.9, 128.29, 128.35, 128.36, 128.62, 128.64, 129.8, 130.1, 132.4, 133.2, 133.3, 133.5, 133.7, 135.3, 136.4, 136.8, 137.9, 138.2, 138.37, 138.42, 138.5, 148.6, 197.1, 197.7, 198.4, 199.1. HRMS calcd for $C_{21}H_{22}O_2Na$: (**mixture**) 329.1512 $[M+Na]^+$, found: 329.1513.

2-Butylidene-1-(4-methoxyphenyl)-4-phenylbutane-1,4-dione (6e)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (75 mg, 78%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.86 (t, *J* = 7.2 Hz, 3H), 1.39-1.43 (m, 2H), 2.14-2.17 (m, 2H), 3.78 (s, 3H), 4.15 (s, 2H), 6.35 (t, *J* = 7.2 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 2H), 7.94 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.9, 22.0, 31.3, 37.4, 55.4, 113.4, 128.3, 128.6, 130.8, 132.1, 133.2, 135.1, 136.8, 146.5, 162.7, 197.1, 197.2. HRMS calcd for $C_{21}H_{22}O_3Na$: 345.1461 $[M+Na]^+$, found: 345.1461.

2-Butylidene-1-(4-fluorophenyl)-4-phenylbutane-1,4-dione (6f)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (56 mg, 60%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.86 (t, *J* = 7.2 Hz, 3H), 1.39-1.43 (m, 2H), 2.15-2.19 (m, 2H), 4.16 (s, 2H), 6.36 (t, *J* = 7.2 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 2H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.76 (d, *J* = 6.6 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.9, 22.0, 31.3, 37.1, 115.2 (d, $^2J_{C\text{-}F}$ = 21.9 Hz), 128.3, 128.7, 132.3 (d, $^3J_{C\text{-}F}$ = 8.9 Hz), 133.3, 135.3, 136.7, 147.6, 165.1 (d, $^1J_{C\text{-}F}$ = 269.1 Hz), 196.9,

197.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ: (major) -107.5; (minor) -105.7. HRMS calcd for $C_{20}H_{19}FO_2Na$: 333.1261 $[M+Na]^+$, found: 333.1237.

2-Butylidene-4-phenyl-1-(thiophen-2-yl)butane-1,4-dione (6g)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (58 mg, 65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92-0.99 (m, 3H), 1.51-1.57 (m, 2H), 2.24-2.29 (m, 2H), 4.21 (s, 2H), 6.75 (t, J = 7.2 Hz, 1H), 7.12-7.14 (m, 1H), 7.45-7.48 (m, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.63 (dd, J_1 = 4.8 Hz, J_2 = 1.2 Hz, 1H), 7.72 (dd, J_1 = 3.6 Hz, J_2 = 1.2 Hz, 1H), 8.00-8.02 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 13.9, 22.1, 31.3, 37.5, 127.6, 128.3, 128.6, 133.1, 133.2, 133.8, 135.2, 136.7, 143.2, 145.5, 189.4, 196.7. HRMS calcd for $C_{18}H_{18}O_2SNa$: 321.0920 $[M+Na]^+$, found: 321.0928.

2-Butylidene-1-phenyl-4-(thiophen-2-yl)butane-1,4-dione (6h)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (56 mg, 63%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: (**major**) 0.94 (t, J = 7.6 Hz, 3H), 1.46-1.52 (m, 2H), 2.26-2.31 (m, 2H), 4.17 (s, 2H), 6.51 (t, J = 7.6 Hz, 1H), 7.14-7.16 (m, 1H), 7.43 (td, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 2H), 7.50 (t, J = 5.2 Hz, 1H), 7.64 (dd, J_1 = 5.2 Hz, J_2 = 1.2 Hz, 1H), 7.74-7.76 (m, 2H), 7.86 (dd, J_1 = 4.0 Hz, J_2 = 1.2 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: (**mixture**) 13.6, 13.9, 21.9, 22.3, 31.5, 32.3, 37.4, 46.2, 128.1, 128.2, 128.5, 129.5, 129.7, 131.7, 132.4, 132.5, 132.9, 133.7, 134.7, 138.4, 138.8, 143.8, 149.1, 189.8, 198.1. HRMS calcd for $C_{18}H_{18}O_2SNa$: (**mixture**) 321.0920 $[M+Na]^+$, found: 321.0933.

2-Butylidene-1,6-diphenylhexane-1,4-dione (6i)

Eluent: ethyl acetate/petroleum ether (1:20); yellow liquid (63 mg, 66%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: (**major**) 0.91 (t, J = 7.2 Hz, 3H), 1.41-1.46 (m, 2H), 2.12-2.17 (m, 2H), 2.77-2.94 (m, 4H), 3.58 (s, 2H), 6.45 (t, J = 7.6 Hz, 1H), 7.13-7.20 (m, 2H), 7.23-7.29 (m, 2H), 7.39-7.55 (m, 4H), 7.67-7.69 (m, 1H), 7.93 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H). (**minor**) 0.74 (t, J = 7.2 Hz, 3H), 1.27-1.32 (m, 2H), 1.76-1.80 (m, 2H), 2.77-2.94 (m, 4H), 3.51 (s, 2H), 5.82 (t, J = 7.6 Hz, 1H), 7.13-7.20 (m, 2H), 7.23-7.29 (m, 4H),

7.39-7.55 (m, 2H), 7.67-7.69 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: (**mixture**) 13.6, 13.9, 21.9, 22.3, 29.5, 29.7, 29.8, 31.4, 32.2, 41.1, 43.9, 44.2, 49.7, 126.1, 128.1, 128.3, 128.4, 128.52, 128.54, 129.4, 129.5, 131.7, 133.0, 133.1, 134.9, 138.2, 138.3, 138.7, 141.0, 141.1, 149.1, 198.1, 198.9, 206.7, 207.3. HRMS calcd for $C_{22}H_{25}O_2$: (**mixture**) 321.1849 $[M+H]^+$, found: 321.1829.

2. Typical procedure for the preparation of *N*,*N*-diethyl-2-(4-methyl-2,5-diphenyl-furan-3-yl)-acetamide (7a)

To a flask containing 2-methyl-1-phenylbuta-2,3-dien-1-ol (**1a'**, 48 mg, 0.3 mmol) and iodobenzene (**2a**, 67 μL, 0.6 mmol) in CH_3CN (2 mL) was added $PdCl_2$ (5 mg, 0.03 mmol), PivOH (12 mg, 0.12 mmol) and NEt_3 (**3a**, 208 μL, 1.5 mmol). The mixture was then stirred at 80 ºC under CO atmosphere (1 atm). Upon completion, the reaction was quenched with aqueous NaCl and extracted with ethyl acetate (10 mL × 3). The combined organic layers were washed with water and brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum and the crude product was purified by column chromatography on silica-gel to afford **7a** in 70% yield. Other furan derivatives **7b-7bb** were prepared in a similar manner.

***N*,*N*-Diethyl-2-(4-methyl-2,5-diphenyl-furan-3-yl)-acetamide (7a)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (73 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.17 (t, *J* = 7.2 Hz, 6H), 2.27 (s, 3H), 3.37 (q, *J* = 7.2 Hz, 2H), 3.45 (q, *J* = 7.2 Hz, 2H), 3.69 (s, 2H), 7.28-7.34 (m, 2H), 7.43 (t, *J* = 7.6 Hz, 4H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.2, 13.1, 14.2, 29.9, 40.7, 42.3, 118.0, 119.1, 125.7, 126.5, 126.7, 127.4, 128.5, 128.6, 131.3, 131.8, 148.0, 149.2, 169.2. HRMS calcd for $C_{23}H_{25}NO_2Na$: 370.1777 $[M+Na]^+$, found: 370.1778.

***N*,*N*-Diethyl-2-(5-(4-methoxyphenyl)-4-methyl-2-phenylfuran-3-yl)acetamide (7b)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (85 mg, 75%); ^{1}H NMR (600 MHz, $CDCl_3$) δ:

1.08 (t, J = 7.2 Hz, 6H), 2.14 (s, 3H), 3.28 (q, J = 7.2 Hz, 2H), 3.36 (q, J = 7.2 Hz, 2H), 3.59 (s, 2H), 3.78 (s, 3H), 6.89 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H), 7.23 (t, J = 7.8 Hz, 1H), 7.33 (t, J = 7.8 Hz, 2H), 7.51 (d, J = 7.2 Hz, 2H), 7.55 (dd, J_1 = 7.2 Hz, J_2 = 1.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 10.1, 13.1, 14.2, 30.0, 40.7, 42.3, 55.3, 114.0, 117.5, 117.9, 124.8, 126.4, 127.22, 127.24, 128.6, 131.4, 148.1, 148.6, 158.6, 169.2. HRMS calcd for $C_{24}H_{28}NO_3$: 378.2064 $[M+H]^+$, found: 378.2063.

_N_,_N_-Diethyl-2-(4-methyl-2-phenyl-5-_p_-tolylfuran-3-yl)acetamide (7c)

Eluent: ethyl acetate/petroleum ether (1:10); yellow solid (70 mg, 65%), mp 120-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.11-1.17 (m, 6H), 2.23 (s, 3H), 2.38 (s, 3H), 3.36 (q, J = 7.2 Hz, 2H), 3.45 (q, J = 7.2 Hz, 2H), 3.66 (s, 2H), 7.22-7.31 (m, 2H), 7.38-7.43 (m, 3H), 7.57-7.60 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.1, 13.1, 14.2, 21.2, 29.9, 40.6, 42.2, 117.9, 118.4, 125.7, 126.4, 127.3, 128.4, 128.5, 129.1, 131.3, 136.5, 148.2, 148.8, 169.2. HRMS calcd for $C_{24}H_{28}NO_2$: 362.2115 $[M+H]^+$, found: 362.2112.

_N_,_N_-Diethyl-2-(5-(4-fluorophenyl)-4-methyl-2-phenylfuran-3-yl)acetamide (7d)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (66 mg, 60%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.09 (t, J = 7.2 Hz, 6H), 2.14 (s, 3H), 3.29 (q, J = 7.2 Hz, 2H), 3.36 (q, J = 7.2 Hz, 2H), 3.58 (s, 2H), 7.03 (t, J = 7.8 Hz, 2H), 7.23 (t, J = 7.8 Hz, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.50 (d, J = 7.8 Hz, 2H), 7.57 (t, J = 6.6 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 10.1, 13.1, 14.3, 29.8, 40.7, 42.3, 115.5 (d, $^2J_{C\text{-}F}$ = 21.9 Hz), 118.0, 118.7, 126.5, 127.45 (d, $^3J_{C\text{-}F}$ = 7.7 Hz), 127.50, 128.1 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 128.6, 131.2, 147.2, 149.2, 161.7 (d, $^1J_{C\text{-}F}$ = 245.1 Hz), 169.1. ^{19}F NMR (565 MHz, $CDCl_3$) δ: -115.0. HRMS calcd for $C_{23}H_{24}FNO_2Na$: 388.1683 $[M+Na]^+$, found: 388.1689.

2-(5-(3-Bromophenyl)-4-methyl-2-phenylfuran-3-yl)-_N_,_N_-diethylacetamide (7e)

Eluent: ethyl acetate/petroleum ether (1:10); yellow solid (79 mg, 62%), mp 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.16 (t, J = 7.2 Hz, 6H), 2.04 (s, 3H), 3.35 (q, J = 7.2 Hz, 2H), 3.45 (q, J = 7.2 Hz, 2H), 3.70 (s, 2H), 7.24-7.49 (m, 6H), 7.62 (d, J = 7.6 Hz, 2H), 7.69 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz,

$CDCl_3$) δ: 9.9, 13.1, 14.2, 30.3, 40.7, 42.3, 116.7, 120.8, 123.6, 126.5, 127.1, 127.5, 128.6, 129.7, 131.2, 132.2, 132.4, 133.3, 147.4, 150.0, 169.2. HRMS calcd for $C_{23}H_{24}BrNO_2Na$: 448.0883 $[M+Na]^+$, found: 448.0881.

***N*,*N*-Diethyl-2-(4-methyl-2-phenyl-5-o-tolylfuran-3-yl)acetamide (7f)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (43 mg, 40%); ^1H NMR (400 MHz, $CDCl_3$) δ: 1.15-1.19 (m, 6H), 2.05 (s, 3H), 2.44 (s, 3H), 3.36 (q, *J* = 7.2 Hz, 2H), 3.45 (q, *J* = 7.2 Hz, 2H), 3.71 (s, 2H), 7.27-7.32 (m, 4H), 7.42 (t, *J* = 7.6 Hz, 3H), 7.59 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.6, 13.1, 14.2, 20.7, 30.3, 40.7, 42.3, 116.8, 119.7, 125.4, 126.3, 127.3, 128.1, 128.6, 130.1, 130.6, 130.7, 131.4, 137.6, 149.0, 149.3, 169.3. HRMS calcd for $C_{24}H_{28}NO_2$: 362.2115 $[M+H]^+$, found: 362.2119.

2-(5-(2-Chlorophenyl)-4-methyl-2-phenylfuran-3-yl)-*N*,*N*-diethylacetamide (7g)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (54 mg, 47%); ^1H NMR (400 MHz, $CDCl_3$) δ: 1.11-1.20 (m, 6H), 2.05 (s, 3H), 3.35 (q, *J* = 7.2 Hz, 2H), 3.44 (q, *J* = 7.2 Hz, 2H), 3.70 (s, 2H), 7.28-7.32 (m, 2H), 7.40-7.43 (m, 3H), 7.48-7.52 (m, 2H), 7.62 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.9, 13.1, 14.2, 30.2, 40.7, 42.3, 116.9, 121.2, 126.48, 126.50, 127.5, 128.58, 128.62, 129.4, 130.1, 131.2, 131.9, 133.6, 146.1, 150.2, 169.2. HRMS calcd for $C_{23}H_{25}ClNO_2$: 382.1568 $[M+H]^+$, found: 382.1567.

2-(5-(3,4-Dimethoxyphenyl)-4-methyl-2-phenylfuran-3-yl)-*N*,*N*-diethylacetamide (7h)

Eluent: ethyl acetate/petroleum ether (1:5); yellow solid (67 mg, 55%), mp 136-137 °C; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.13-1.17 (m, 6H), 2.22 (s, 3H), 3.35 (q, *J* = 7.6 Hz, 2H), 3.43 (q, *J* = 7.2 Hz, 2H), 3.65 (s, 2H), 3.91 (s, 3H), 3.93 (s, 3H), 6.92 (d, *J* = 7.6 Hz, 1H), 7.20-7.31 (m, 3H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.1, 13.1, 14.2, 29.9, 40.6, 42.2, 55.9, 109.3, 111.1, 117.8, 117.9, 118.6, 124.9, 126.4, 127.3, 128.5, 131.3, 148.0, 148.1, 148.6, 148.9, 169.2. HRMS

calcd for $C_{25}H_{30}NO_4$: 408.2169 $[M+H]^+$, found: 408.2172.

_N_,_N_-Diethyl-2-(4-methyl-2-phenyl-5-(thiophen-2-yl)furan-3-yl)acetamide (7i)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (82 mg, 77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.16 (t, J = 6.8 Hz, 6H), 2.23 (s, 3H), 3.35 (q, J = 7.2 Hz, 2H), 3.44 (q, J = 7.2 Hz, 2H), 3.66 (s, 2H), 7.10 (t, J = 4.0 Hz, 1H), 7.27-7.34 (m, 3H), 7.42 (dd, J_1 = 7.6 Hz, J_2 = 4.0 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.9, 13.1, 14.3, 29.8, 40.6, 42.3, 117.9, 118.7, 122.8, 123.8, 126.4, 127.5, 128.6, 129.1, 131.1, 134.0, 144.4, 148.9, 169.1. HRMS calcd for $C_{21}H_{24}NO_2S$: 354.1522 $[M+H]^+$, found: 354.1524.

(*E*)-*N*,*N*-Diethyl-2-(4-methyl-2-phenyl-5-styrylfuran-3-yl)acetamide (7j)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (93 mg, 83%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.14-1.19 (m, 6H), 2.13 (s, 3H), 3.34 (q, J = 6.8 Hz, 2H), 3.44 (q, J = 7.2 Hz, 2H), 3.65 (s, 2H), 6.96 (d, J = 16.4 Hz, 1H), 7.09 (d, J = 16.4 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.34-7.39 (m, 3H), 7.45 (t, J = 7.6 Hz, 2H), 7.52 (d, J = 7.6 Hz, 2H), 7.63 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.9, 13.1, 14.2, 29.9, 40.7, 42.3, 114.7, 117.7, 121.8, 125.6, 126.2, 126.5, 127.2, 127.6, 128.6, 128.7, 131.1, 137.6, 148.1, 149.6, 169.1. HRMS calcd for $C_{25}H_{27}NO_2Na$: 396.1934 $[M+Na]^+$, found: 396.1934.

(*Z*)-2-(5-(2,6-Dimethylhepta-1,5-dienyl)-4-methyl-2-phenylfuran-3-yl)-*N*,*N*-diethylacetamide (7k)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (92 mg, 78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.11-1.14 (m, 6H), 1.59-1.65 (m, 4H), 1.70 (s, 3H), 1.98 (s, 3H), 2.12 (s, 3H), 2.19 (s, 3H), 3.32 (q, J = 7.2 Hz, 2H), 3.40 (q, J = 7.2 Hz, 2H), 3.62 (s, 2H), 5.14-5.15 (m, 1H), 6.00 (s, 1H), 7.25-7.26 (m, 1H), 7.36-7.40 (m, 2H), 7.54 (dd, J_1 = 8.4 Hz, J_2 = 0.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.8, 13.1, 14.1, 17.7, 18.6, 25.7, 26.8, 30.0, 40.5, 41.2, 42.2, 111.7, 116.7, 119.4, 123.9, 125.9, 126.9, 128.5, 137.5, 148.2, 148.6, 169.1. HRMS calcd for $C_{26}H_{36}NO_2$: 394.2741 $[M+H]^+$, found: 394.2743.

2-(5-Benzyl-4-methyl-2-phenylfuran-3-yl)-*N*,*N*-diethylacetamide (7l)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (81 mg, 75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.11-1.18 (m, 6H), 2.00 (s, 3H), 3.32 (q, *J* = 7.2 Hz, 2H), 3.43 (q, *J* = 7.2 Hz, 2H), 3.63 (s, 2H), 4.02 (s, 2H), 7.22-7.33 (m, 6H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.7, 13.1, 14.2, 30.1, 32.5, 40.6, 42.2, 116.3, 118.0, 126.2, 127.1, 128.47, 128.49, 131.5, 138.8, 148.5, 148.6, 169.3. HRMS calcd for $C_{24}H_{28}NO_2$: 362.2115 $[M+H]^+$, found: 362.2109.

***N*,*N*-Diethyl-2-(4-methyl-5-phenethyl-2-phenylfuran-3-yl)acetamide (7m)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (87 mg, 77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.07-1.14 (m, 6H), 1.81 (s, 3H), 2.91-2.98 (m, 4H), 3.26-3.40 (m, 4H), 3.58 (s, 2H), 7.19-7.21 (m, 3H), 7.25-7.30 (m, 2H), 7.37-7.40 (m, 3H), 7.50 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.3, 13.0, 14.1, 28.4, 30.1, 34.8, 40.5, 42.2, 116.1, 117.2, 125.9, 126.1, 126.3, 126.9, 128.3, 128.4, 128.5, 141.5, 148.1, 149.6, 169.3. HRMS calcd for $C_{25}H_{29}NO_2Na$: 398.2090 $[M+Na]^+$, found: 398.2086.

***N*,*N*-Diethyl-2-(4-methyl-2-phenyl-5-propylfuran-3-yl)acetamide (7n)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (69 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.95 (t, *J* = 7.2 Hz, 3H), 1.06-1.14 (m, 6H), 1.67 (q, *J* = 7.2 Hz, 2H), 1.93 (s, 3H), 2.58 (t, *J* = 7.2 Hz, 2H), 3.28 (q, *J* = 7.2 Hz, 2H), 3.39 (q, *J* = 7.6 Hz, 2H), 3.60 (s, 2H), 7.24 (t, *J* = 7.2 Hz, 1H), 7.35-7.39 (m, 2H), 7.49 (dd, J_1 = 8.4 Hz, J_2 = 0.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 8.5, 13.0, 13.8, 14.0, 21.9, 28.2, 30.2, 40.6, 42.2, 116.0, 116.7, 126.0, 126.8, 128.4, 131.8, 147.8, 150.7, 169.5. HRMS calcd for $C_{20}H_{27}NO_2Na$: 336.1934 $[M+Na]^+$, found: 336.1926.

***N*,*N*-Diethyl-2-(4-ethyl-2-phenyl-5-*p*-tolylfuran-3-yl)acetamide (7o)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow solid (77 mg, 68%), mp 90-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.16-1.20 (m, 6H), 1.27 (t, *J* = 7.6 Hz, 3H), 2.40 (s, 3H), 2.69 (q, *J* = 7.6 Hz, 2H), 3.38 (q, *J* = 7.6 Hz, 2H), 3.46 (q, *J* = 7.2 Hz, 2H), 3.68 (s, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 8.4 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.1, 14.3, 14.5,

17.6, 21.3, 29.7, 40.8, 42.3, 117.3, 124.6, 125.5, 126.4, 127.3, 128.5, 129.1, 129.3, 131.4, 136.6, 147.9, 149.2, 169.3. HRMS calcd for $C_{25}H_{30}NO_2$: 376.2271 $[M+H]^+$, found: 376.2277.

2-(5-Benzyl-4-ethyl-2-phenylfuran-3-yl)-*N*,*N*-diethylacetamide (7p)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (79 mg, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.09-1.18 (m, 9H), 2.44 (q, J = 7.6 Hz, 2H), 3.32 (q, J = 7.6 Hz, 2H), 3.42 (q, J = 7.2 Hz, 2H), 3.63 (s, 2H), 4.02 (s, 2H), 7.22-7.33 (m, 6H), 7.36-7.39 (m, 2H), 7.51 (dd, J_1 = 8.4 Hz, J_2 = 4.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.1, 14.1, 15.2, 17.0, 30.0, 32.6, 40.7, 42.2, 115.6, 124.1, 126.2, 126.3, 127.0, 128.46, 128.48, 131.5, 138.9, 148.4, 148.9, 169.5. HRMS calcd for $C_{25}H_{29}NO_2Na$: 398.2090 $[M+Na]^+$, found: 398.2094.

***N*,*N*-Diethyl-2-(4-ethyl-5-phenethyl-2-phenylfuran-3-yl)acetamide (7q)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (78 mg, 67%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.97-1.13 (m, 9H), 2.29 (q, J = 8.0 Hz, 2H), 2.91-3.00 (m, 4H), 3.29 (q, J = 7.2 Hz, 2H), 3.39 (q, J = 6.8 Hz, 2H), 3.58 (s, 2H), 7.17-7.21 (m, 3H), 7.26-7.30 (m, 3H), 7.39 (t, J = 7.6 Hz, 2H), 7.52 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.0, 14.1, 15.1, 16.8, 28.6, 29.9, 35.0, 40.6, 42.2, 115.4, 123.3, 125.9, 126.2, 126.9, 128.3, 128.4, 128.5, 131.6, 141.6, 148.3, 149.5, 169.4. HRMS calcd for $C_{26}H_{32}NO_2$: 390.2428 $[M+H]^+$, found: 390.2430.

***N*,*N*-Diethyl-2-(2,4,5-triphenylfuran-3-yl)acetamide (7r)**

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (43 mg, 35%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.95 (t, J = 7.2 Hz, 3H), 1.12 (t, J = 7.2 Hz, 3H), 3.09 (q, J = 7.2 Hz, 2H), 3.39 (q, J = 7.2 Hz, 2H), 3.46 (s, 2H), 7.18-7.51 (m, 10H), 7.63 (t, J = 7.6 Hz, 1H), 7.78 (d, J = 7.6 Hz, 2H), 8.12 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.0, 14.0, 29.5, 30.9, 40.9, 42.1, 117.9, 125.4, 126.3, 127.0, 127.55, 127.62, 128.3, 128.4, 128.6, 128.8, 130.2, 130.3, 131.1, 133.6, 147.5, 150.1, 169.6. HRMS calcd for $C_{28}H_{27}NO_2Na$: 432.1934 $[M+Na]^+$, found: 432.1937.

2-(5-(3,4-Dimethoxyphenyl)-2-(4-methoxyphenyl)-4-methylfuran-3-yl)-*N*,*N*-diethylacetamide (7s)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (59 mg, 45%); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 1.06-1.09 (m, 6H), 2.14 (s, 3H), 3.27 (q, J = 6.6 Hz, 2H), 3.35 (q, J = 6.6 Hz, 2H), 3.55 (s, 2H), 3.77 (s, 3H), 3.84 (s, 3H), 3.86 (s, 3H), 6.85 (d, J = 8.4 Hz, 1H), 6.88 (dd, J_1 = 6.6 Hz, J_2 = 1.2 Hz, 2H), 7.12-7.14 (m, 2H), 7.45 (dd, J_1 = 6.6 Hz, J_2 = 1.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 10.2, 13.1, 14.2, 30.0, 40.6, 42.3, 55.3, 55.9, 109.3, 111.2, 114.1, 116.7, 117.6, 118.6, 124.2, 125.1, 128.0, 147.6, 148.0, 148.8, 148.9, 159.1, 169.4. HRMS calcd for $C_{26}H_{32}NO_5$: 438.2275 $[M+H]^+$, found: 438.2277.

2-(5-(3,4-Dimethoxyphenyl)-2-(4-fluorophenyl)-4-methylfuran-3-yl)-*N*,*N*-diethylacetamide (7t)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (93 mg, 73%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.13-1.20 (m, 6H), 2.20 (s, 3H), 3.36-3.44 (m, 4H), 3.61 (s, 2H), 3.92 (s, 3H), 3.93 (s, 3H), 6.92 (d, J = 8.8 Hz, 1H), 7.10 (t, J = 8.0 Hz, 2H), 7.19-7.20 (m, 2H), 7.54-7.58 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.0, 13.1, 14.3, 29.7, 40.7, 42.2, 55.9, 109.4, 111.2, 115.5 (d, $^{2}J_{C\text{-}F}$ = 21.4 Hz), 117.6, 118.7, 124.8, 127.6, 128.2 (d, $^{3}J_{C\text{-}F}$ = 7.6 Hz), 147.95, 148.04, 148.9, 169.1. ^{19}F NMR (565 MHz, $CDCl_3$) δ: -114.1. HRMS calcd for $C_{25}H_{29}FNO_4$: 426.2075 $[M+H]^+$, found: 426.2075.

2-(2-(2-Chlorophenyl)-5-(3,4-dimethoxyphenyl)-4-methylfuran-3-yl)-*N*,*N*-diethylacetamide (7u)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (73 mg, 55%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.04-1.11 (m, 6H), 2.24 (s, 3H), 3.25 (q, J = 7.2 Hz, 2H), 3.36 (q, J = 7.2 Hz, 2H), 3.46 (s, 2H), 3.90 (s, 3H), 3.91 (s, 3H), 6.91 (d, J = 8.0 Hz, 1H), 7.19-7.32 (m, 4H), 7.46-7.50 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.3, 13.0, 14.1, 29.9, 40.6, 42.2, 55.8, 55.9, 109.3, 111.0, 116.9, 118.6, 120.1, 124.9, 126.6, 129.6, 130.09, 130.13, 132.0, 133.8, 146.1, 148.1, 148.8, 148.9, 169.1. HRMS calcd for $C_{25}H_{28}ClNO_4Na$: 464.1599 $[M+Na]^+$, found: 464.1612.

***N*,*N*-Diethyl-2-(5-(4-methoxyphenyl)-4-methyl-2-(m-tolyl)furan-3-yl)acetamide (7v)**

Eluent: ethyl acetate/petroleum ether (1:10); yellow solid (83 mg, 71%), mp 97-98 °C; ^{1}H NMR (400

MHz, $CDCl_3$) δ: 1.14-1.18 (m, 6H), 2.21 (s, 3H), 2.39 (s, 3H), 3.35 (q, J = 6.8 Hz, 2H), 3.43 (q, J = 6.8 Hz, 2H), 3.65 (s, 2H), 3.84 (s, 3H), 6.96 (dd, J_1 = 6.8 Hz, J_2 = 2.4 Hz, 2H), 7.11 (d, J = 7.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 7.37-7.38 (m, 2H), 7.62 (dd, J_1 = 6.8 Hz, J_2 = 2.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.0, 13.1, 14.2, 21.5, 30.0, 40.6, 42.2, 55.3, 113.9, 117.6, 117.7, 123.5, 124.8, 126.9, 127.2, 128.0, 128.4, 131.3, 138.1, 147.9, 148.6, 158.5, 169.3. HRMS calcd for $C_{25}H_{30}NO_3$: 392.2220 $[M+H]^+$, found: 392.2219.

_N_,_N_-Diethyl-2-(4-methyl-2,5-di(thiophen-2-yl)furan-3-yl)acetamide (7w)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (57 mg, 53%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.14-1.21 (m, 6H), 2.21 (s, 3H), 3.36-3.44 (m, 4H), 3.69 (s, 2H), 7.08-7.10 (m, 2H), 7.27-7.30 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 9.9, 13.1, 14.3, 29.9, 40.6, 42.3, 117.8, 118.8, 123.0, 124.02, 124.05, 124.6, 127.4, 127.5, 132.8, 133.7, 144.2, 144.3, 168.5. HRMS calcd for $C_{19}H_{22}NO_2S_2$: 360.1086 $[M+H]^+$, found: 360.1091.

2-(5-Benzyl-4-ethyl-2-phenylfuran-3-yl)-_N_,_N_-dibutylacetamide (7x)

Eluent: ethyl acetate/petroleum ether (1:10); yellow liquid (110 mg, 85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.89-0.96 (m, 6H), 1.11 (t, J = 7.6 Hz, 3H), 1.20-1.34 (m, 4H), 1.51-1.56 (m, 4H), 2.44 (q, J = 7.6 Hz, 2H), 3.25 (t, J = 7.6 Hz, 2H), 3.37 (t, J = 7.6 Hz, 2H), 3.63 (s, 2H), 4.02 (s, 2H), 7.24-7.39 (m, 8H), 7.51 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.87, 13.93, 15.2, 17.0, 20.1, 20.3, 29.8, 30.0, 31.2, 32.6, 46.1, 48.0, 115.7, 124.1, 126.20, 126.22, 127.0, 128.4, 128.47, 128.50, 131.5, 138.9, 148.3, 148.9, 169.8. HRMS calcd for $C_{29}H_{38}NO_2$: 432.2897 $[M+H]^+$, found: 432.2896.

_N_-Ethyl-_N_-methyl-2-(4-methyl-2,5-diphenylfuran-3-yl)acetamide (7y)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (30 mg, 30%); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.13-1.20 (m, 3H), 2.26 (s, 3H), 3.02 (d, 3H), 3.39 (q, J = 7.2 Hz, 1H), 3.50 (q, J = 6.8 Hz, 1H), 3.68 (d, 2H), 7.28-7.34 (m, 2H), 7.44 (t, J = 7.6 Hz, 4H), 7.62 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H). ^{13}C

NMR (100 MHz, $CDCl_3$) δ: 10.2, 12.4, 13.4, 29.7, 30.2, 33.1, 35.0, 42.9, 44.5, 117.8, 117.9, 119.0, 119.1, 125.7, 126.4, 126.5, 126.8, 127.4, 127.5, 128.4, 128.5, 128.6, 131.28, 131.33, 131.8, 148.0, 149.2, 169.5, 169.7. HRMS calcd for $C_{22}H_{24}NO_2$: 334.1802 $[M+H]^+$, found: 334.1795.

_N_-Ethyl-2-(5-(4-methoxyphenyl)-4-methyl-2-phenylfuran-3-yl)-_N_-methylacetamide (7z)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (47 mg, 43%); ^1H NMR (600 MHz, $CDCl_3$) δ: 1.02-1.06 (m, 3H), 2.11 (s, 3H), 2.89 (d, 3H), 3.26 (q, J = 7.2 Hz, 1H), 3.38 (q, J = 7.2 Hz, 1H), 3.57 (d, 2H), 3.74 (s, 3H), 6.86 (d, J = 8.4 Hz, 2H), 7.19 (t, J = 7.8 Hz, 1H), 7.31 (t, J = 7.8 Hz, 2H), 7.49 (d, J = 7.8 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 10.1, 12.4, 13.4, 29.7, 30.3, 33.1, 35.0, 42.9, 44.6, 55.3, 114.0, 117.5, 117.6, 117.69, 117.71, 124.8, 126.30, 126.34, 127.19, 127.23, 127.3, 128.3, 128.6, 130.0, 131.4, 131.5, 148.10, 148.12, 148.58, 148.60, 158.6, 169.7, 169.8. HRMS calcd for $C_{23}H_{26}NO_3$: 364.1907 $[M+H]^+$, found: 364.1900.

_N,N_-Diisopropyl-2-(4-methyl-2,5-diphenylfuran-3-yl)acetamide (7aa)

Eluent: ethyl acetate/petroleum ether (1:5); yellow solid (78 mg, 69%), mp 89-90 °C; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.14 (d, J = 6.4 Hz, 6H), 1.44 (d, J = 6.4 Hz, 6H), 2.28 (s, 3H), 3.42-3.44 (m, 1H), 3.67 (s, 2H), 3.98-4.01 (m, 1H), 7.27-7.34 (m, 2H), 7.42-7.46 (m, 4H), 7.61 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 7.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.2, 20.6, 20.7, 32.2, 46.1, 48.8, 118.3, 119.3, 125.7, 126.4, 126.7, 127.4, 128.5, 128.6, 131.4, 131.9, 148.0, 148.9, 168.6. HRMS calcd for $C_{25}H_{30}NO_2$: 376.2271 $[M+H]^+$, found: 376.2270.

2-(4-Ethyl-2-phenyl-5-(_p_-tolyl)furan-3-yl)-_N,N_-diisopropylacetamide (7bb)

Eluent: ethyl acetate/petroleum ether (1:5); yellow liquid (79 mg, 65%); ^1H NMR (400 MHz, $CDCl_3$) δ: 1.00 (d, J = 6.8 Hz, 6H), 1.28 (t, J = 7.2 Hz, 3H), 1.42 (d, J = 7.2 Hz, 6H), 2.40 (s, 3H), 2.70 (q, J = 7.6 Hz, 2H), 3.43 (s, 1H), 3.65 (s, 2H), 4.02-4.05 (m, 1H), 7.24-7.32 (m, 3H), 7.42 (t, J = 7.6 Hz, 2H), 7.62 (d, J = 7.6 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.5, 17.6, 20.6, 20.8, 21.3, 31.8, 46.0, 48.6, 117.5,

124.6, 125.6, 126.3, 127.2, 127.8, 128.5, 129.2, 131.4, 136.6, 148.0, 148.9, 168.9. HRMS calcd for $C_{27}H_{33}NO_2Na$: 426.2404 $[M+Na]^+$, found: 426.2408.

3. Control Experiments

3.1. To a flask containing 2-methyl-1-phenylbuta-2,3-dien-1-ol (**1a'**, 48 mg, 0.3 mmol) and iodobenzene (**2a**, 67 μL, 0.6 mmol) in CH_3CN (2 mL) was added $PdCl_2$ (5mg, 0.03 mmol), PivOH (12 mg, 0.12 mmol) and Et_2NH (**8**, 154 μL, 1.5 mmol). The mixture was then stirred at 80 ºC under CO atmosphere (1 atm) for 8 h. Afterwards, it was diluted with aqueous NH_4Cl (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1:10) as the eluent to give **7a** (37 mg, 36%).

3.2. To a flask containing 2-methyl-1-phenylbuta-2,3-dien-1-ol (**1a'**, 48 mg, 0.3 mmol) and iodobenzene (**2a**, 67 μL, 0.6 mmol) in CH_3CN (2 mL) was added $PdCl_2$ (5mg, 0.03 mmol), PivOH (12 mg, 0.12 mmol), NEt_3 (**3a**, 208 μL, 1.5 mmol) and 4Å molecule sieves (**300** mg). The mixture was then stirred at 80 ºC under CO atmosphere (1 atm) for 8 h. Afterwards, it was diluted with aqueous NH_4Cl (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/petroleum ether (1:10) as the eluent to give **7a** (16 mg, 15%).

3.3. To a flask containing 2-methyl-1-phenylbuta-2,3-dien-1-ol (**1a'**, 48 mg, 0.3 mmol) and iodobenzene (**2a**, 67 μL, 0.6 mmol) in CH_3CN (2 mL) was added $PdCl_2$ (5mg, 0.03 mmol), PivOH (12 mg, 0.12 mmol), NEt_3 (**3a**, 208 μL, 1.5 mmol) and H_2O (162 μL, 9 mmol). The mixture was then stirred at 80 ºC under CO atmosphere (1 atm) for 8 h. Afterwards, it was diluted with aqueous NH_4Cl (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica

gel with EtOAc/petroleum ether (1:10) as the eluent to give **7a** (70 mg, 67%).

Supporting Information. Copies of ^{1}H and ^{13}C NMR spectra of all products and the ^{1}H-^{1}H NOSEY spectra of **4** and **6**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

Acknowledgments. We are grateful to the National Natural Science Foundation of China (NSFC) (Grant No 21702050), Key Science and Technology Project in Henan Province (172102310590) for financial support.

References

(1) (a) Friis, S. D.; Lindhardt, A. T.; Skrydstrup, T. The Development and Application of Two-Chamber Reactors and Carbon Monoxide Precursors for Safe Carbonylation Reactions. *Acc. Chem. Res.* **2016**, *49*, 594-605. (b) Liu, Q.; Zhang, H.; Lei, A. Oxidative Carbonylation Reactions: Organometallic Compounds (R-M) or Hydrocarbons (R-H) as Nucleophiles. *Angew. Chem., Int. Ed.* **2011**, *50*, 10788-10799. (c) Li, Y.; Wang, Z.; Wu, X.-F. A Sustainable Procedure toward Alkyl Arylacetates: Palladium-Catalysed Direct Carbonylation of Benzyl Alcohols in Organic Carbonates. *Green Chem.* **2018**, *20*, 969-972 and references cited therein.

(2) (a) Ye, J.; Ma, S. Palladium-Catalyzed Cyclization Reactions of Allenes in the Presence of Unsaturated Carbon−Carbon Bonds. *Acc. Chem. Res.* **2014**, *47*, 989-1000. (b) Bras, J. L.; Muzart, J. Palladium-Catalysed Inter- and Intramolecular Formation of C–O Bonds from Allenes. *Chem. Soc. Rev.* **2014**, *43*, 3003-3040. (c) Dai, J.; Wang, M.; Chai, G.; Fu, C.; Ma, S. A Practical Solution to Stereodefined Tetrasubstituted Olefins. *J. Am. Chem. Soc.* **2016**, *138*, 2532-2535 and references cited therein.

(3) He, Y.; Zhang, X.; Fan, X. Synthesis of Diversely Substituted 2-(Furan-3-yl)acetates from Allenols through Cascade Carbonylations. *Chem. Commun.* **2015**, *51*, 16263-16266.

(4) (a) Tye, J. W.; Weng, Z.; Johns, A. M.; Incarvito, C. D.; Hartwig, J. F. Copper Complexes of Anionic Nitrogen Ligands in the Amidation and Imidation of Aryl Halides. *J. Am. Chem. Soc.*

2008, *130*, 9971-9983. (b) Giri, R.; Hartwig, J. F. Cu(I)-Amido Complexes in the Ullmann Reaction: Reactions of Cu(I)-Amido Complexes with Iodoarenes with and without Autocatalysis by CuI. *J. Am. Chem. Soc.* **2010**, *132*, 15860-15863.

(5) (a) Widenhoefer, R. A.; Buchwald, S. L. Halide and Amine Influence in the Equilibrium Formation of Palladium Tris(*o*-tolyl)phosphine Mono(amine) Complexes from Palladium Aryl Halide Dimers. *Organometallics* **1996**, *15*, 2755-2763. (b) Widenhoefer, R. A.; Buchwald, S. L. Formation of Palladium Bis(amine) Complexes from Reaction of Amine with Palladium Tris(*o*-tolyl)phosphine Mono(amine) Complexes. *Organometallics* **1996**, *15*, 3534-3542. (c) Shi, R.; Zhang, H.; Lu, L.; Gan, P.; Sha, Y.; Zhang, H.; Liu, Q.; Belle, M.; Lei, A. (*E*)-α,β-Unsaturated Amides from Tertiary Amines, Olefins and CO *via* Pd/Cu-Catalyzed Aerobic Oxidative *N*-Dealkylation. *Chem. Commun.* **2015**, *51*, 3247-3250.

(6) (a) Ouyang, K.; Hao, W.; Zhang, W.-X.; Xi, Z. Transition-Metal-Catalyzed Cleavage of C−N Single Bonds. *Chem. Rev.* **2015**, *115*, 12045-12090. (b) Wang, Q.; Su, Y.; Li, L.; Huang, H. Transition-Metal Catalysed C–N Bond Activation. *Chem. Soc. Rev.* **2016**, *45*, 1257-1272. (c) Mane, R. S.; Bhanage, B. M. Carbonylative Tertiary Amide Synthesis from Aryl Iodides and Tertiary Amines *via* Oxidant-Free C-N Bond Cleavage Catalyzed by Palladium(II) Chloride in Polyethylene Glycol/Water. *Adv. Synth. Catal.* **2017**, *359*, 2621-2629.

(7) (a) Shi, R.; Lu, L.; Xie, H.; Yan, J.; Xu, T.; Zhang, H.; Qi, X.; Lan, Y.; Lei, A. C8-H Bond Activation *vs*. C2-H Bond Activation: from Naphthyl Amines to Lactams. C*hem. Commun.* **2016**, *52*, 13307-13310. (b) Gao, B.; Huang, H. Palladium-Catalyzed Hydroaminocarbonylation of Alkynes with Tertiary Amines *via* C−N Bond Cleavage. *Org. Lett.* **2017**, *19*, 6260-6263 and references cited therein. (c) Mane, R. S.; Bhanage, B. M. Ligand-Assisted Pd-Catalyzed *N*-Dealkylative Carbonylation of Tertiary Amines with (Hetero)Aryl Halides to Tertiary Amides. *Asian J. Org. Chem.* **2018**, *7*, 160-164 and references cited therein.

(8) (a) Zhou, L.; Stewart, G.; Rideau, E.; Westwood, N. J.; Smith, T. K. A Class of 5-Nitro-2-furancarboxylamides with Potent Trypanocidal Activity against *Trypanosoma brucei* in Vitro. *J. Med. Chem.* **2013**, *56*, 796-806. (b) Parenti, M. D.; Grozio, A.; Bauer, I.; Galeno, L.; Damonte, P.; Millo, E.; Sociali, G.; Franceschi, C.; Ballestrero, A.; Bruzzone, S.; Rio, A. D.; Nencioni, A. Discovery of Novel and Selective SIRT6 Inhibitors. *J. Med. Chem.* **2014**, *57*, 4796-4804. (c) Jacques, S. A.; Kuhn, I.; Koniev, O.; Schuber, F.; Lund, F. E.; Wagner, A.; Muller-Steffner, H.; Kellenberger, E. Discovery of Potent Inhibitors of *Schistosoma mansoni* NAD^+ Catabolizing Enzyme. *J. Med. Chem.* **2015**, *58*, 3582-3592. (d) Nagase, H.; Yamamoto, N.; Yata, M.; Ohrui, S.; Okada, T.; Saitoh, T.; Kutsumura, N.; Nagumo, Y.; Irukayama-Tomobe, Y.; Ishikawa, Y.; Ogawa, Y.; Hirayama, S.; Kuroda, D.; Watanabe, Y.; Gouda, H.; Yanagisawa, M. Design and Synthesis of Potent and Highly Selective Orexin 1 Receptor Antagonists with a Morphinan Skeleton and Their Pharmacologies. *J. Med. Chem.* **2017**, *60*, 1018-1040. (e) Jiménez-Somarribas, A.; Mao, S.; Yoon, J.-J.; Weisshaar, M.; Cox, R. M.; Marengo, J. R.; Mitchell, D. G.; Morehouse, Z. P.; Yan, D.; Solis, I.; Liotta, D. C.; Natchus, M. G.; Plemper, R. K. Identification of Non-Nucleoside Inhibitors of the Respiratory Syncytial Virus Polymerase Complex. *J. Med. Chem.* **2017**, *60*, 2305-2325. (f) Yu, Y.; Zheng, J.; Cao, L.; Li, S.; Li, X.; Zhou, H.-B.; Liu, X.; Wu, S.; Dong, C. Furan-Carboxamide Derivatives as Novel Inhibitors of Lethal H5N1 Influenza A Viruses. *RSC Adv.* **2017**, *7*, 9620-9627.

(9) (a) García-Álvarez, R.; Zablocka, M.; Crochet, P.; Duhayon, C.; Majoral, J.-P.; Cadierno, V. Thiazolyl-Phosphine Hydrochloride Salts: Effective Auxiliary Ligands for Ruthenium-Catalyzed Nitrile Hydration Reactions and Related Amide Bond forming Processes in Water. *Green Chem.* **2013**, *15*, 2447-2456. (b) Molander, G. A.; Traister, K. M.; Barcellos, T. Palladium-Catalyzed α-Arylation of 2-Chloroacetates and 2-Chloroacetamides. *J. Org. Chem.* **2013**, *78*, 4123-4131. (c) González-Liste, P. J.; Cadierno, V.; García-Garrido, S.

E. Catalytic Rearrangement of Aldoximes to Primary Amides in Environmentally Friendly Media under Thermal and Microwave Heating: Another Application of the Bis(allyl)-Ruthenium(IV) Dimer [{RuCl(μ-Cl)(η^3:η^3-$C_{10}H_{16}$)}$_2$]. *ACS Sustainable Chem. Eng.* **2015**, *3*, 3004-3011. (d) González-Fernández, R.; Crochet, P.; Cadierno, V.; Menéndez, M. I.; López, R. Phosphinous Acid-Assisted Hydration of Nitriles: Understanding the Controversial Reactivity of Osmium and Ruthenium Catalysts. *Chem. Eur. J.* **2017**, *23*, 15210-15221. (e) Rajesh, M.; Puri, S.; Kant, R.; Reddy, M. S. Synthesis of Substituted Furan/Pyrrole-3-carboxamides through a Tandem Nucleopalladation and Isocyanate Insertion. *Org. Lett.* **2016**, *18*, 4332-4335.

(10) (a) Rao, H. S. P.; Jothilingam, S. Facile Microwave-Mediated Transformations of 2-Butene-1,4-diones and 2-Butyne-1,4-diones to Furan Derivatives. *J. Org. Chem.* **2003**, *68*, 5392-5394. (b) Rao, H. S. P.; Senthilkumar, S. P. Domino Michael-Aldol Reactions on 1,4-Diarylbut-2-ene-1,4-diones with Methyl Acetoacetate Furnish Methyl 2-Aroyl-4-hydroxy-6-oxo-4-arylcyclohexane-1-carboxylate Derivatives. *J. Org. Chem.* **2004**, *69*, 2591-2594. (c) Wahl, B.; Lee, D. S.; Woodward, S. 1,4-Addition of $TMSCCl_3$ to (*E*)-Fumaric Esters and Thermal Rearrangement of the Adducts to 3,4-Dichloropent-2-enedioates. *Eur. J. Org. Chem.* **2015**, 6033-6039. (d) Olson, M. E.; Abate-Pella, D.; Perkins, A. L.; Li, M.; Carpenter, M. A.; Rathore, A.; Harris, R. S.; Harki, D. A. Oxidative Reactivities of 2-Furylquinolines: Ubiquitous Scaffolds in Common High-Throughput Screening Libraries. *J. Med. Chem.* **2015**, *58*, 7419-7430. (e) He, Y.; Tian, M.-M.; Zhang, X.-Y.; Fan, X.-S. Synthesis of 4-Oxo-but-2-enals through ^{t}BuONO and TEMPO Promoted Cascade Reactions of Homoallylic Alcohols. *Asian J. Org. Chem.* **2016**, *5*, 1318-1322.

(11) (a) Aly, A. H.; Edrada-Ebel, R.; Indriani, I. D.; Wray, V.; Müller, W. E. G.; Totzke, F.; Zirrgiebel, U.; Schächtele, C.; Kubbutat, M. H. G.; Lin, W. H.; Proksch, P.; Ebel, R. Cytotoxic

Metabolites from the Fungal Endophyte Alternaria sp. and Their Subsequent Detection in Its Host Plant *Polygonum senegalense*. *J. Nat. Prod.* **2008**, *71*, 972-980. (b) Zhong, W.; Springstead, J. R.; Al-Mubarak, R.; Lee, S.; Li, R.; Emert, B.; Berliner, J. A.; Jung, M. E. An Epoxyisoprostane Is a Major Regulator of Endothelial Cell Function. *J. Med. Chem.* **2013**, *56*, 8521-8532. (c) Singh, G.; Meyer, A.; Aubé, J. Stereodivergent Synthesis of Enantioenriched 4□Hydroxy-2-Cyclopentenones. *J. Org. Chem.* **2014**, *79*, 452-458. (d) Ma, D.; Fu, C.; Ma, S. Diastereoselective Construction of Cyclopent-2-enone-4-ols from Aldehydes and 1,2-Allenones Catalyzed by *N*-Heterocyclic Carbine. *Chem. Commun.* **2016**, *52*, 14426-14429.

(12) FajarÍ, L.; Brillas, E.; Alemán, C.; Juliá, L. α-Linked Bifuran and α,α'-Linked Tricycles Containing Furan and/or Thiophene. EPR Investigations and Electrochemical Behavior. *J. Org. Chem.* **1998**, *63*, 5324-5331.

(13) (a) Larock, R. C.; Berrios-Peña, N.; Narayanan, K. Palladium-Catalyzed Heteroannulation of 1,3-Dienes by Functionally Substituted Aryl Halides. *J. Org. Chem.* **1990**, *55*, 3447-3450. (b) Liu, S.; Zhao, J.; Zhang, G. Regio- and Stereoselective Synthesis of Functionalized Allylic Fluorides *via* Palladium-Catalyzed Three-Component Tandem Carbofluorination of Allenes. *Tetrohendron Lett.* **2015**, *56*, 2214-2218.

(14) Zhang, G.; Gao, B.; Huang, H. Palladium-Catalyzed Hydroaminocarbonylation of Alkenes with Amines: A Strategy to Overcome the Basicity Barrier Imparted by Aliphatic Amines. *Angew. Chem., Int. Ed.* **2015**, *54*, 7657-7661.

(15) (a) Kuang, J.; Ma, S. An Efficient Synthesis of Terminal Allenes from Terminal 1-Alkynes. *J. Org. Chem*. **2009**, *74*, 1763-1765. (b) Webster, S.; Young, P. C.; Barker, G.; Rosair, G. M.; Lee, A.-L. Dehydrative Thiolation of Allenols: Indium *vs* Gold Catalysis. *J. Org. Chem*. **2015**, *80*, 1703-1718.

(16) Wu, W.-L.; Yao, Z.-J.; Li, Y.-L.; Li, J.-C.; Xia, Y.; Wu, Y.-L. Diastereoselective Propargylation of α-Alkoxy Aldehydes with Propargyl Bromide and Zinc. A Versatile and

Efficient Method for the Synthesis of Chiral Oxygenated Acyclic Natural Products. *J. Org. Chem*. **1995**, *60*, 3257-3259.

(17) Lutz, R. E.; Taylor, R. J. Studies on Unsaturated 1,4-Dicarbonyl Compounds. VII. Aryl Unsaturated 1,4-Diketones and Ketonic Acids Derived from Citraconic and Mesaconic Acids, with Particular Reference to the *β*-[*p*-Bromobenzoyl]-methylacrylic Acids. *J. Am. Chem. Soc.* **1933**, *55,* 1168-1178.

(18) Bailey, P. S.; Bath, S. S.; Thomsen, W. F.; Nelson, H. H.; Kawas, E. E. Preparations and Reactions with Amines of Some 1,2-Dibenzoylalkene. *J. Org. Chem*. **1956**, *21,* 297-303.