JOC The Journal of Organic Chemistry

Article

Copper-Catalyzed [2 + 3] Cyclization of #-Hydroxyl Ketones and Arylacetonitriles: Access to Multisubstituted Butenolides and Oxazoles

Chaorong Qi, Youbin Peng, Lu Wang, Yanwei Ren, and Huanfeng Jiang

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b01822 • Publication Date (Web): 03 Sep 2018

Just Accepted

ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

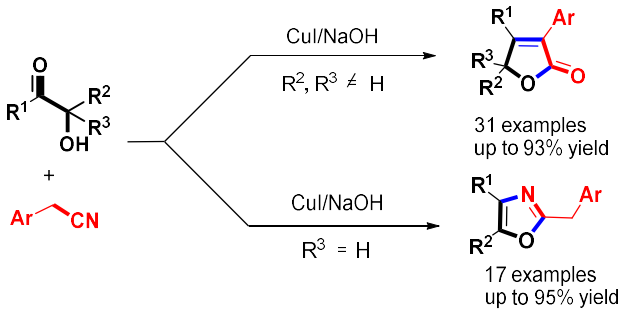
Copper-Catalyzed [2 + 3] Cyclization of α-Hydroxyl Ketones and Arylacetonitriles: Access to Multisubstituted Butenolides and Oxazoles

Chaorong Qi,*[a,b] Youbin Peng,[a] Lu Wang,[a] Yanwei Ren[a] and Huanfeng Jiang*[a]

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

[b] State Key Lab of Luminescent Materials and Devices, South China University of Technology, Guangzhou 510640, P. R. China

E-mail: crqi@scut.edu.cn or jianghf@scut.edu.cn



Abstract: A copper-catalyzed [2 + 3] formal cyclization reaction between α-hydroxyl ketones and arylacetonitriles has been developed. The reaction outcome was ultimately dependent on the structure of the α-hydroxy ketones employed. Tertiary α-hydroxy ketones gave 3,4,5,5-tetrasubstituted butenolides as the sole products while secondary α-hydroxy ketones furnished 2,4,5-trisubstituted oxazoles selectively. This method has many advantages, such as the use of easily available substrates, broad substrate scope, good functional tolerance and milder reaction conditions.

INTRODUCTION

Both butenolides and oxazoles are important five-membered heterocycles, which have

been found as key structural units in a great number of biologically active natural products and pharmaceutically important molecules.[1,2] For example, both cadiolide C[1d] and ramariolide A[1e] are butenolide-containing molecules, which exhibit significant antibacterial activity and *in vitro* antimicrobial activity against *Mycobacterium smegmatis* and *Mycobacterium tuberculosis*, respectively; ulapualide C bearing three oxazole cycles was isolated from egg masses of the nudibranch *Hexabranchus sanguineus* and was found to have potential cytotoxicity against select NCI cell lines (**Figure 1**).[2e] Additionally, butenolides and oxazoles are also valuable synthetic intermediates for the construction of a variety of important complex molecules.[3,4] Therefore, the development of efficient methodologies for the synthesis of these heteroaromatic compounds is of great importance in organic synthesis and medicinal chemistry.

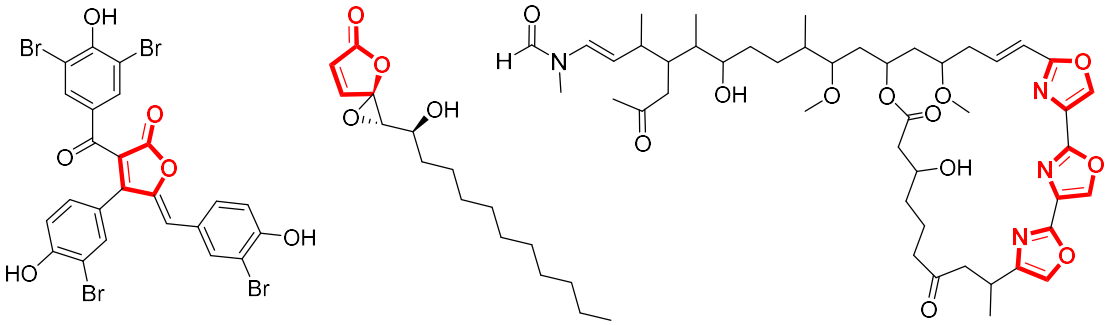


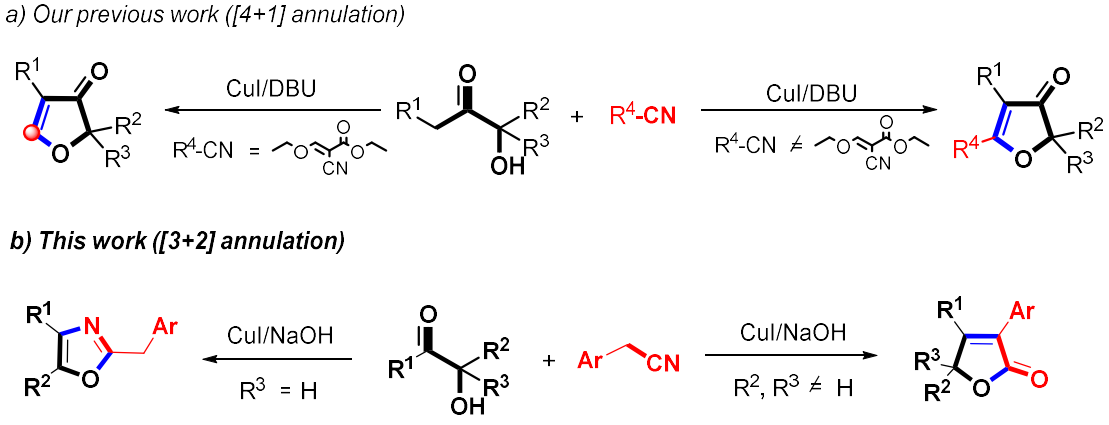
Figure 1. Representative natural products containing butenolide or oxazole moiety.

Traditionally, multi-substituted butenolides and oxazoles were constructed through transition metal-catalyzed or metal-free intramolecular cyclization strategies.[5,6] Recently, many elegant intermolecular cyclization reactions have been developed for the synthesis of these heterocycles.[7,8] For example, Shindo and co-workers reported a Cu(II)-catalyzed tandem acylation-Wittig reaction of acyloins

with a thiol ester leading to a one-pot synthesis of butenolides under neutral conditions.[7b] Zhu et al. successfully developed a synergistic acid-promoted synthesis of highly substituted butenolides via the annulation of keto acids and tertiary alcohols.[7e]And very recently, Lin et al. reported a DBU-catalyzed [3 + 2] annulation of cyclopropenones and β-ketoesters, providing a direct approach to highly functionalized butenolides with a quaternary center.[7f] In regard to the synthesis of oxozales, Xiao's group reported a novel [3+2] cycloaddition/oxidative aromatization of 2*H*-azirines and aldehydes via visible light-induced photoredox catalysis to produce 2,4,5-trisubstituted oxazoles.[8g] Davies et al. have developed a gold-catalyzed regioselective annulations of alkynyl thioethers with aminides to form densely functionalized oxazoles.[8i] Although great progress have been made in these fields, the development of new and facile procedures that allow the synthesis of structurally diverse butenolides and oxazoles via intermolecular annulations strategies using easily available substrates as the starting materials is still highly desirable.

In 2016, we have developed a copper-catalyzed [4 + 1] annulations reaction between α-hydroxy ketones and nitriles for the construction of a wide range of 3(2*H*)-furanone derivatives, in which the product structure relied on the nature of nitriles (Scheme 1, a).[9a] As part of our continuous interest in the use of α-hydroxyl ketones and nitriles as versatile building blocks in the organic synthesis,[9] herein, we wish to report a copper-catalyzed [2 + 3] cyclization of α-hydroxyl ketones and arylacetonitriles for the synthesis of a variety of highly substituted butenolides and oxazoles (Scheme 1, b).

Scheme 1. Annulation between α-hydroxy ketones and nitriles

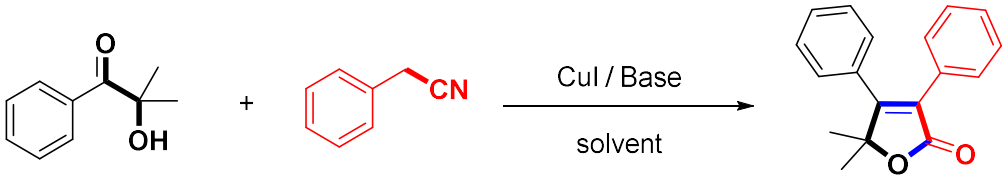


RESULTS AND DISCUSSION

Our initial efforts focused on the formal [2+3] annulation reaction of 2-hydroxy-2-methyl-1-phenylpropan-1-one (**1a**) and 2-phenylacetonitrile (**2a**) to obtain 5,5-dimethyl-3,4-diphenylfuran-2(5*H*)-one (**3aa**), and the results were summarized in Table 1. On the basis of our previous work,[9a] we performed the reaction using CuI as the catalyst in the presence of 0.5 equiv of DBU in methanol at 80 °C under N_2 atmosphere, but no trace of the desired product **3aa** was detected (entry 1). The use of *t*-BuOK instead of DBU as the base did not give **3aa** either (entry 2). However, when the reaction was conducted in a mixed MeOH-H_2O (1:1) solvent, the target product **3aa** was formed in 36% yield (entry 3), while the use of neat water as the reaction media only led to a very low yield (entry 4). To our delight, the yield of **3aa** could be increased to 83% by increasing the amount of *t*-BuOK to 1 equiv and prolonging the reaction time to 24 h. These results prompted us to further investigate other organic or inorganic base and it was showed that the nature of the base has great influence on the transformation. In comparison with *t*-BuOK, NaOH

was more efficient for the annulation but the use of other bases such as Et_3N, DABCO, DMAP, CH_3ONa or Cs_2CO_3 would lead to no or lower yield of **3aa** (entries 6-11). Pleasingly, the yield of the desired product **3aa** could be improved to 90% when 1.2 equivalent of NaOH was employed (entry 12). Two more control experiments showed that both copper salt and base are necessary for the reaction to proceed smoothly (entries 13 and 14). Other copper salts such as CuCl, CuBr, $Cu(OAc)_2$ and $Cu(OTf)_2$ were also examined and all of them could catalyze the reaction to give the desired product albeit in slightly lower yields (entries 15-18). The results also showed that the volume ratio of MeOH/H_2O has influence on the reaction, and a MeOH/H_2O ratio of 1:1 was found to be optimal (entries 12, 19 and 20). It should be noted that the reaction could proceed smoothly to give **3aa** in 82% yield even when the loading of catalyst was reduced to 5 mol% (entry 21).

Table 1. Optimization of the reaction [a]



1a **2a** **3aa**

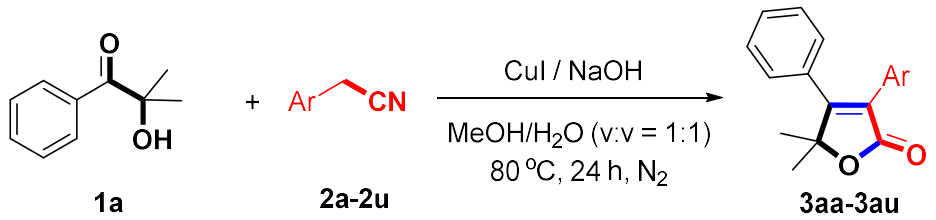
Entry	Catalyst	Base (equiv)	Solvent (v:v)	Time (h)	Yield (%) [b]
1	CuI	DBU (0.5)	MeOH	12	n.d.
2	CuI	*t*-BuOK (0.5)	MeOH	12	n.d.
3	CuI	*t*-BuOK (0.5)	MeOH/H_2O (1:1)	12	36
4	CuI	*t*-BuOK (0.5)	H_2O	12	8
5	CuI	*t*-BuOK (1)	MeOH/H_2O (1:1)	24	83
6	CuI	Et_3N (1)	MeOH/H_2O (1:1)	24	trace

7	CuI	DABCO (1)	MeOH/H_2O (1:1)	24	n.d.
8	CuI	DMAP (1)	MeOH/H_2O (1:1)	24	n.d.
9	CuI	Cs_2CO_3 (1)	MeOH/H_2O (1:1)	24	47
10	CuI	CH_3ONa (1)	MeOH/H_2O (1:1)	24	64
11	CuI	NaOH (1)	MeOH/H_2O (1:1)	24	86
12	CuI	**NaOH (1.2)**	**MeOH/H_2O (1:1)**	**24**	**90 (88)**
13	CuI	-	MeOH/H_2O (1:1)	24	n.d.
14	-	NaOH (1.2)	MeOH/H_2O (1:1)	24	51
15	CuCl	NaOH (1.2)	MeOH/H_2O (1:1)	24	85
16	CuBr	NaOH (1.2)	MeOH/H_2O (1:1)	24	87
17	$Cu(OAc)_2$	NaOH (1.2)	MeOH/H_2O (1:1)	24	86
18	$Cu(OTf)_2$	NaOH (1.2)	MeOH/H_2O (1:1)	24	83
19	CuI	NaOH (1.2)	MeOH/H_2O (3:1)	24	80
20	CuI	NaOH (1.2)	MeOH/H_2O (1:3)	24	73
21[c]	CuI	NaOH (1.2)	MeOH/H_2O (1:1)	24	82

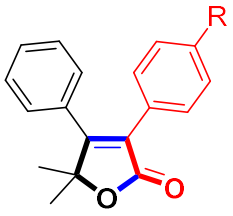
[a] Reaction conditions: **1a** (0.3 mmol), **2a**(0.6 mmol), CuI (0.03 mmol), solvent (2 mL), 80 ^oC, 24 h, N_2 atmosphere. [b] Yield were determined by GC-MS analysis with *n*-dodecane as internal standard. Number in parentheses is the yield of isolated product. [c] The reaction was performed in the presence of 0.015 mmol of CuI.

With the optimized reaction conditions in hand, the copper-catalyzed formal [2+3] annulation was then applied to the reaction of **1a** with various arylacetonitriles. As can be seen from Table 2, a wide range of arylacetonitriles with different substitution patterns could undergo the reaction to give the corresponding products (**3aa**-**3aj**) in moderate to excellent yields. Both electron-donating and -withdrawing groups at the *para*-position of the benzene ring, including halide (F, Cl, Br, I), alkyl (Me and ^{t}Bu),

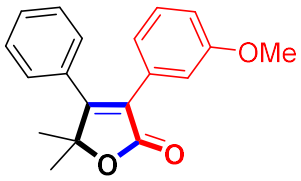
Table 2. Scope of arylacetonitriles [a]



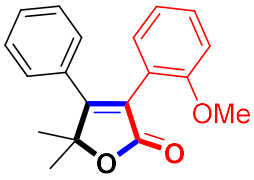
1a **2a-2u** **3aa-3au**



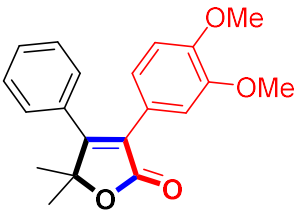
3aa, R = H, 88%
3ab, R = F, 68%
3ac, R = Cl, 78%
3ad, R = Br, 80%
3ae, R = I, 61%
3af, R = Me, 90%
3ag, R = ^{t}Bu, 82%
3ah, R = OMe, 79%
3ai, R = CF_3, 82%
3aj, R = NO_2, 50%



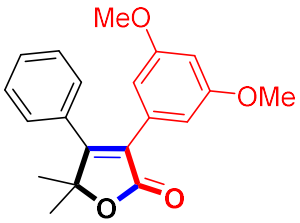
3ak, 88%



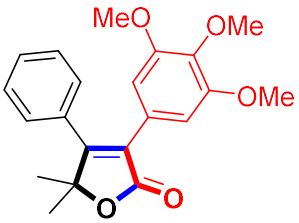
3al, 85%



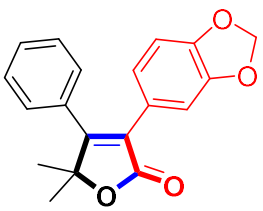
3am, 71% (62%)[b]



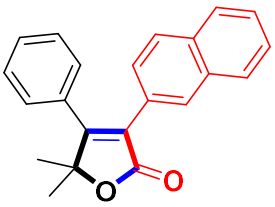
3an, 74%



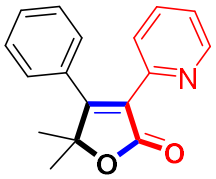
3ao, 50%



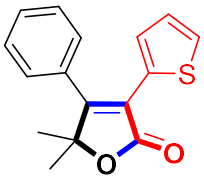
3ap, 74%



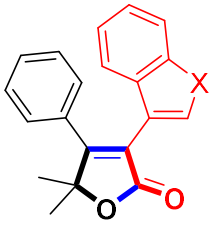
3aq, 81%



3ar, 93%



3as, 87%



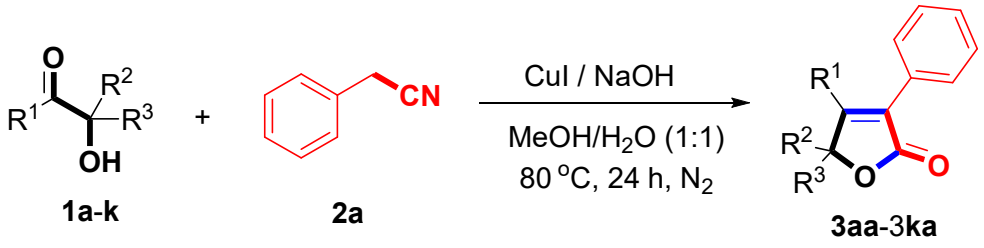
3at, X = S, 70%
3au, X = O, 56%

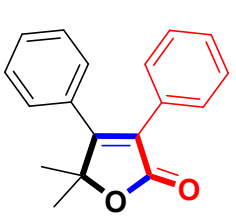
[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.6 mmol), CuI (0.03 mmol), NaOH (0.36 mmol), MeOH/H_2O (v:v = 1:1, 2 mL), 80 °C, 24 h, N_2 atmosphere. Isolated yield based on **1a**. [b] The reaction was performed on a 5 mmol scale.

methoxy, trifluoromethyl, and even nitro group were tolerated without any difficulty under the reaction conditions, which would provide ample potential for further transformations. The structure of the product **3ad** was unambiguously confirmed by means of X-ray crystallographic analysis (Figure S1).[10] Moreover, it was found that the steric hindrance has little influence on the transformation as *ortho*- or *meta*-substituted substrates could furnish the corresponding products (**3ak** and **3al**) in high yields as well. In addition to mono-substituted arylacetonitriles, di- or tri-substituted ones reacted well with **1a** to afford the desired products (**3am**-**3ao**). Moreover, product **3am** could be obtained in a satisfactory yield (62%) when the reaction was conducted on a 5 mmol scale, demonstrating the scalability of the present reaction. To our delight, the nitriles containing heterocycles or fused aryl rings (**2p**-**2u**) could be successfully transformed into the corresponding products **3ap**-**3au**. However, alkyl nitriles such as butyronitrile could not take part in the reaction, and could be recovered unchanged after the experiment (not showed).

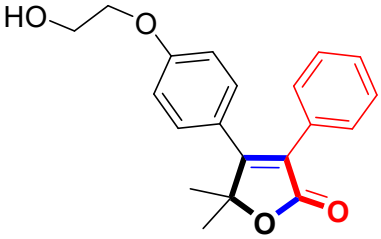
Subsequently, the reactivity of various α-hydroxy ketones was examined (Table 3). Gratifyingly, a range of aryl and heteroaryl-substituted tertiary α-hydroxy ketones (**1a**-**1e**) could react with 2-phenylacetonitrile (**2a**) smoothly to generate the corresponding products **3aa**-**3ea** in moderate to high yields. The substrate **1b** with a 2-hydroxyethoxy group at position 4 of the benzenyl ring could enter into the reaction and gave the desired product carrying a free hydroxyl group (**3ba**) in a satisfactory yield. Both cyclopentyl and cyclohexyl ring adjacent to the carbonyl group were compatible with the transformation and the spirocyclic products **3ca** and **3da** were

Table 3.Scope of α-hydroxyl ketones[a]

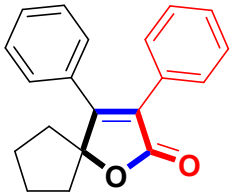




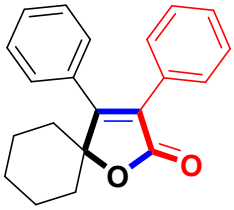
3aa, 88%



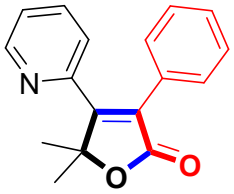
3ba,58%



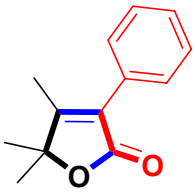
3ca, 64%



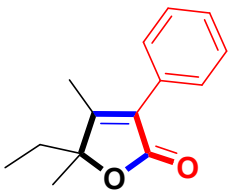
3da, 62%



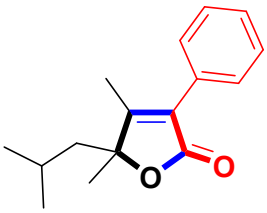
3ea, 80%



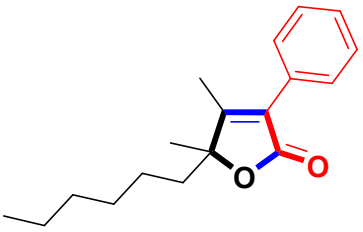
3fa, 63%



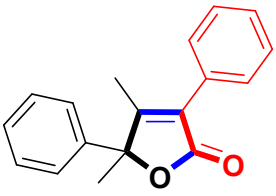
3ga, 73%



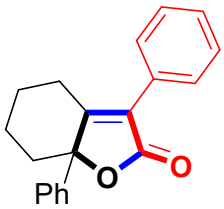
3ha, 40%



3ia, 50%



3ja, 73%



3ka,76%

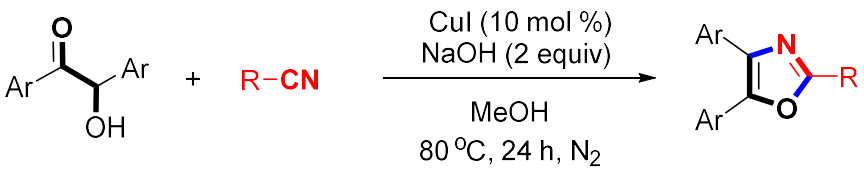
[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.6 mmol), CuI (0.03 mmol), NaOH (0.36 mmol), MeOH/H_2O (v:v = 1:1, 2 mL), 80 °C, 24 h, N_2 atmosphere. Isolated yield based on **1**.

obtained in 64% and 62% yields, respectively. Moreover, the catalytic protocol could be applied to a variety of methyl ketones with different R^2 and R^3 substituents including alkyl and aryl groups, furnishing the corresponding products (**3fa**-**3ja**) in synthetically useful yields. It was notable that 2-hydroxy-2-phenylcyclohexan-1-one (**1k**) was also a good substrate for the reaction and afforded the desired product (**3ka**) with a fused-ring system in a high yield.

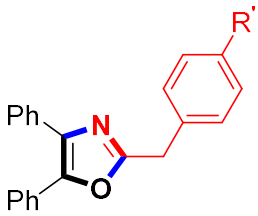
To our surprise, when benzoin (**1m**), which is a secondary α-hydroxy ketone, was used as the substrate to react with **2a** under the standard reaction conditions, no trace of desired butenolide product was detected. However, a 2,4,5-trisubstituted oxazole derivative, 2-benzyl-4,5-diphenyloxazole (**4ma**), was obtained in 28% yield upon isolation. This result indicated that the *gem*-disubstituent effect play a crucial role in the formation of butenolide products,[11] and oxazole ring would be more easy to formed when secondary α-hydroxy ketones were employed for the reaction. Considering that the reaction might provide a straightforward method for the construction of 2-benzyl-substituted oxazoles, which are difficult to be synthesized by previously reported methods,[6,8] we decided to further optimize the reaction. Fortunately, when the reaction media was switched to MeOH and 2 equivalents of NaOH was added as the base, the yield of **4ma** could be dramatically increased to 75%.

Encouraged by this result, the scope of the transformation was then investigated. As can be seen from Table 4, both electron-rich and electron-deficient 2-arylacetonitriles could work well with **1m** to deliver the desired oxazoles in moderate to excellent

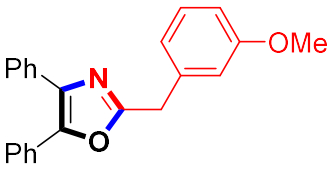
Table 4: Synthesis of 2,4,5-trisubstituted oxazoles [a]



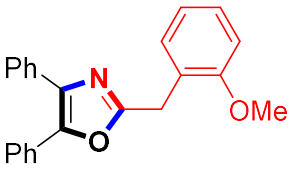
1m-1o **2** **4**



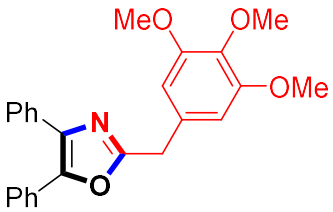
4ma, R' = H, 75% (28%)[b]
4mb, R' = F, 81%
4mc, R' = Cl, 86%
4md, R' = Br, 70%
4me, R' = I, 56%
4mf, R' = Me, 92%
4mh, R' = OMe, 84%
4mi, R' = CF_3, 69%



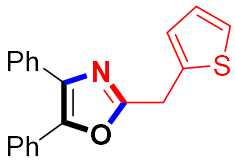
4mk, 68%



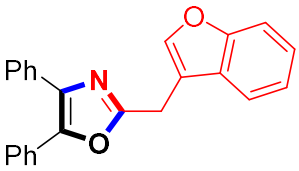
4ml, 55%



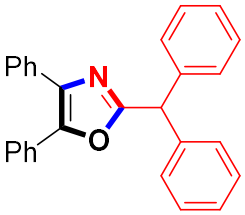
4mo, 71%



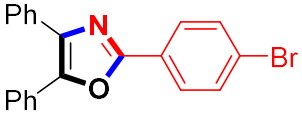
4ms, 32%



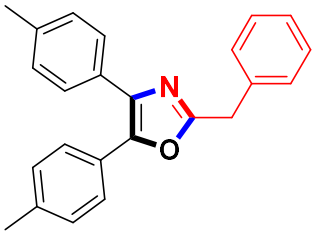
4mu, 73%



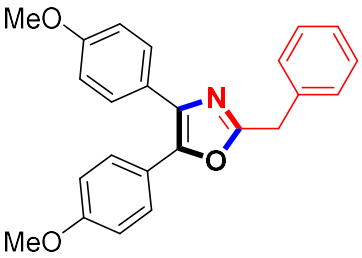
4mw, 95%



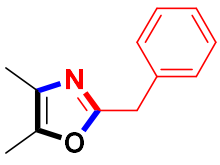
4mx, 23%



4na, 82%



4oa, 93%



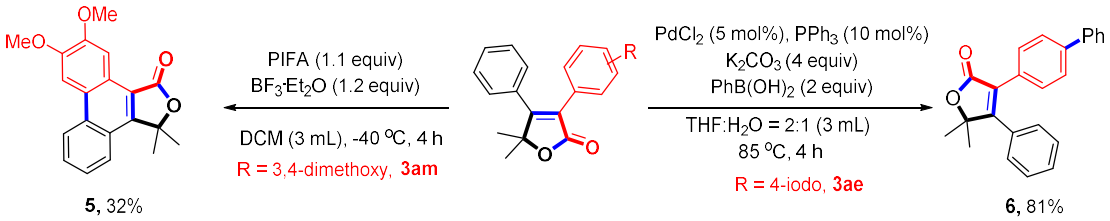
4pa, n.d.[c]

[a] Reaction conditions: **1** (0.3 mmol), **2** (0.6 mmol), CuI (0.03 mmol), NaOH (0.6 mmol), MeOH (1 mL), 80 °C, 24 h, N_2 atmosphere. Isolated yield based on **1**. [b] The reaction was carried out with 0.36 mmol of NaOH in a mixed MeOH/H_2O (v:v = 1:1, 2 mL) solvent. [c] n.d. = not detected.

yields (**4ma**-**4ml**). It was also found that *ortho*-substituted substrate **2l** exhibited lower reactivity than its *para*- and *meta*-substituted analogues, which might be due to the steric hindrance effect. Substrate **2o** having three methoxy group on its benzene ring afforded the desired product **4mo** in 71% yield. Pleasingly, the nitriles containing a heterocycle could also be successfully transformed into the desired products (**4ms** and **4mu**). Notably, when 2,2-diphenylacetonitrile (**2w)** was applied as the reaction partner, excellent yield of **4mw** was obtained. By contrast, benzonitriles showed much lower reactivity to the reaction, as exemplified by 4-bromobenzonitrile (**2x**), which gave the desired product **4mx** in only 23% yield. Other benzoins such as **1n** and **1o** could also react with **2a** efficiently to give the desired products **4na** and **4oa** in 82% and 93% yields, respectively. However, the acyloin **1p** failed to take part in the cyclization reaction but led to the formation of large amount of unidentified products. Alkyl nitriles such as butyronitrile and pentanenitrile also failed to undergo the reaction to give the corresponding oxazole derivatives, and the raw materials could be recovered.

To demonstrate the synthetic utility of the new method, the products derived from this method were employed for further transformations to prepare other functional molecules. As shown in Scheme 2, compound **3am** could enter into Scholl-type oxidative cyclization reaction in the presence of 1.1 equivalents of phenyliodine(III) bis(trifluoroacetate) (PIFA), giving rise to a phenanthrene-fused butenolide derivative **5**, albeit in a low yield.[12] Moreover, compound **3ae** having an iodo-substituted aromatic ring could efficiently undergo Suzuki–Miyaura cross-coupling with phenylboronic acid, furnishing product **6** in 81% yield upon isolation.

Scheme 2. The synthetic utility



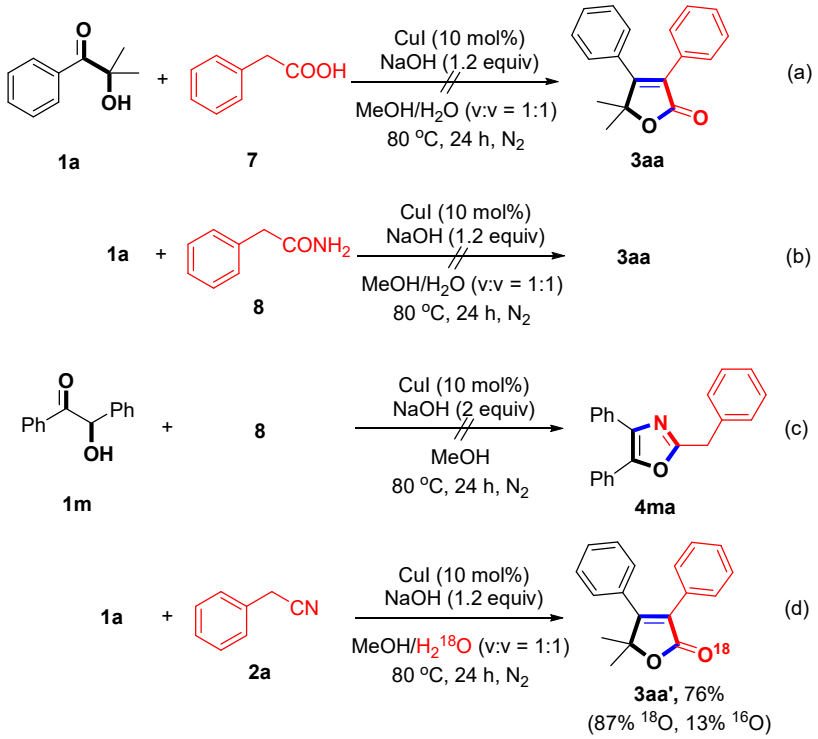
5, 32% **6**, 81%

To obtain more insight into the mechanism of the transformation, a series of control experiments were performed. When phenylacetic acid (**7**) was employed to react with **1a** under the standard reaction conditions, no trace of **3aa** was observed (Scheme 3, a). Moreover, phenylacetamide (**8**) could not undergo the reaction with **1a** or **1m** under the standard conditions to give the desired product **3aa** or **4ma** (Scheme 3, b and c). These results revealed that neither phenylacetic acid nor phenylacetamide is the intermediate of the reaction. Finally, when $H_2{}^{18}O$ was used in the reaction of **1a** and **2a** under the optimized conditions, the ^{18}O-isotopologue **3aa′** was obtained in 76% yield and in 87% isotopic purity (Scheme 3, d). This isotope labeled experiment revealed that water also acted as a reaction participant and the carbonyl oxygen atom of products **3** was mainly originated from water.

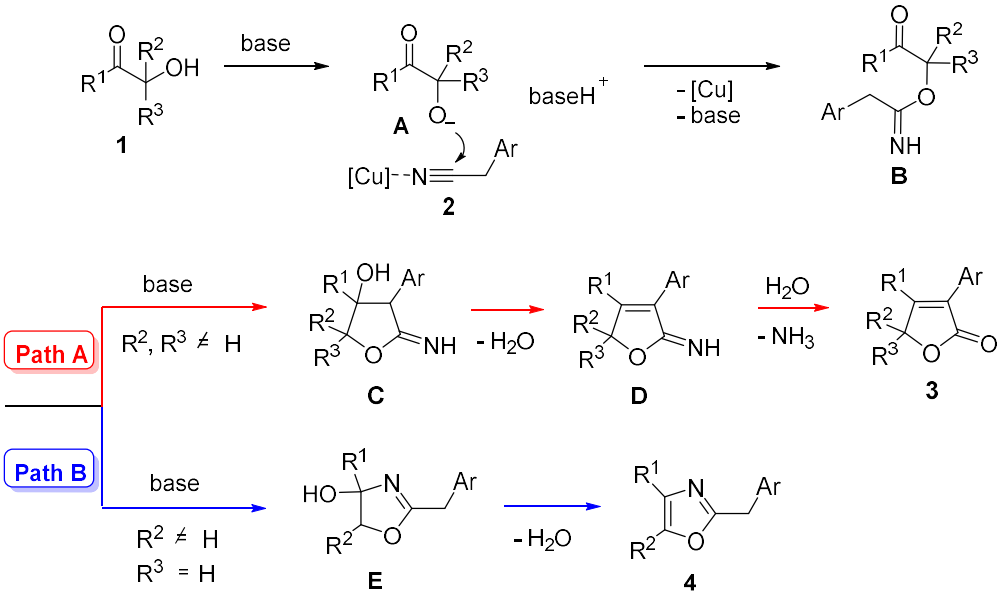
On the basis of the above results and previous literatures,[9a, 10] a plausible mechanism is illustrated in Scheme 4. Initially, under the action of base, α-hydroxy ketones **1** generates an oxy anion species **A**, which would undergo a nucleophilic attack to nitrile **2** activated by copper salt to give intermediate **B**. In the case where neither R^2 nor R^3 is hydrogen atom, intermediate **B** will undergo an intramolecular Knoevenagel reaction to give intermediate **D** via **C** due to the Thorpe-Ingold effect. Then, the hydrolyzation of **D** will give the butenolide product **3** (Path A). However,

when R^3 is a hydrogen atom, intermediate **B** will undergo an intramolecular cyclization to give intermediate **E** instead of **C**. The subsequent dehydration of **E** will give rise to the oxazole product **4** (Path B).

Scheme 3. Mechanism studies



Scheme 4. Plausible mechanism for the reaction



CONCLUSION

In conclusion, we have successfully developed a copper catalyzed [2 + 3] cyclization reaction between α-hydroxy ketones and arylacetonitriles. The outcome of the reaction was dependent on the structure of α-hydroxy ketones: tertiary α-hydroxy ketones afforded the highly substituted butenolide products while the secondary ones selectively gave rise to oxazole derivatives. The protocol features mild reaction conditions, high yields, the use of easily available substrates, a broad substrate scope and good functional group tolerance.

EXPERIMENTAL SECTION

General method. ^{1}H and ^{13}C NMR spectra were recorded using a 400 MHz NMR spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. The chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. GC analyses were performed on a gas chromatograph with an FID and equipped with an AT.SE-30 capillary column (internal diameter: 0.32 mm, length: 30 m). Mass spectra were recorded on a gas chromatograph-mass spectrometer at an ionization voltage of 70 eV and equipped with a DB-WAX capillary column (internal diameter: 0.25 mm, length: 30 m). The data of HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). IR spectra were obtained either as potassium bromide pellets or as liquid films between two potassium bromide pellets with an infrared spectrometer. Melting points were determined with a digital melting point measuring instrument. The α-hydroxy ketones were prepared according to previous literature procedures.[13] Other compounds and solvents were commercially purchased and used without

further purification.

General procedure for the preparation of butenolides 3. To a 25 mL dried Schlenk tube was added the mixture of NaOH (0.36 mmol), CuI (0.03 mmol), tertiary α-hydroxy ketones **1** (0.3 mmol), arylacetonitriles **2** (0.6 mmol), MeOH (1 mL) and H_2O (1 mL) successively. The mixture was then stirred at 80 °C for 24 h under N_2 atomsphere. After the reaction was completed, the mixture was cooled to room temperature, diluted with saturated brine water (15 mL), and extracted with EtOAc (10 mL×3). The organic phase was washed with H_2O (10 mL×3), dried over anhydrous Na_2SO_4, and then filtered. After removing the solvent under vacuum, the crude product was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (20:1 to 10:1) as the eluent to give the desired product **3**.

5,5-Dimethyl-3,4-diphenylfuran-2(*5H*)-one (3aa).[14] Colorless solid (75.8 mg, 88%), mp: 159–161 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (m, 5H), 7.25 – 7.17 (m, 5H), 1.60 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 166.1, 132.5, 129.7, 129.1(3), 129.1(0), 128.9, 128.4, 128.1, 127.8, 126.2, 85.8, 25.3. IR (KBr): 2988, 2927, 1752, 1652, 1495, 1447, 1363, 1281, 1195, 1130, 1015, 964, 756, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{16}NaO_2$ $[M + Na]^+$: 287.1043; found: 287.1046.

3-(4-Fluorophenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ab). Colorless solid (57.5 mg, 68%), mp: 164–166 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.37 (m, 5H), 7.25 – 7.16 (m, 2H), 6.91 (t, J = 8.1 Hz, 2H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 165.9, 162.6 (d, J = 247.6 Hz), 132.4, 131.0 (d, J = 8.2 Hz), 129.3, 129.1, 127.7, 125.7 (d, J = 3.4 Hz), 125.2, 115.2 (d, J = 21.4 Hz), 85.9, 25.2. IR (KBr):

3072, 2988, 2936, 1758, 1599, 1511, 1285, 1225, 1131, 1020, 965, 839, 755, 706 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{15}FNaO_2$ $[M + Na]^+$: 305.0948; found: 305.0951.

3-(4-Chlorophenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ac). Colorless solid (69.7 mg, 78%), mp: 139–141 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (s, 3H), 7.33 (d, J = 7.2 Hz, 2H), 7.19 (d, J = 6.8 Hz, 4H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 166.5, 134.4, 132.2, 130.4, 129.3, 129.1, 128.4, 128.1, 127.6, 125.1, 85.9, 25.2. IR (KBr): 2984, 2923, 1750, 1560, 1943, 1281, 1195, 1131, 1095, 1016, 964, 828, 757, 703 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{15}ClNaO_2$ $[M + Na]^+$: 321.0653; found: 321.0658.

3-(4-Bromophenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ad). Colorless solid (72.9 mg, 80%), mp: 133–135 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.44 – 7.39 (m, 3H), 7.35 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 7.2 Hz, 2H), 7.22 – 7.17 (m, 2H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 166.6, 132.2, 131.3, 130.7, 129.3, 129.1, 128.6, 127.6, 125.2, 122.8, 85.9, 25.2. IR (KBr): 2982, 2923, 1746, 1583, 1488, 1276, 1190, 1012, 960, 886, 821, 753, 702 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{15}BrNaO_2$ $[M + Na]^+$: 365.0148; found: 365.0153.

3-(4-Iodophenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ae). Yellow solid (71.4 mg, 61%), mp: 128–130 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, J = 7.6 Hz, 2H), 7.44 – 7.38 (m, 3H), 7.22 – 7.16 (m, 2H), 7.12 (d, J = 7.6 Hz, 2H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 166.7, 137.3, 132.1, 130.8, 129.3, 129.1(3), 129.0(9), 127.6, 125.2, 94.7, 85.9, 25.2. IR (KBr): 2981, 2930, 1751, 1485, 1213,

1130, 1012, 964, 823, 758, 702 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{15}INaO_2$ [M + Na]$^+$: 413.0009; found: 413.0012.

5,5-Dimethyl-4-phenyl-3-(p-tolyl)furan-2(*5H*)-one (3af). Colorless solid (75.0 mg, 90%), mp: 166–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (s, 3H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.21 (br, 2H), 7.03 (d, *J* = 7.6 Hz, 2H), 2.27 (s, 3H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 165.3, 138.3, 132.7, 130.0, 129.0, 128.9, 128.8, 127.8, 126.7, 126.0, 85.6, 25.3, 21.2. IR (KBr): 2983, 1744, 1445, 1281, 1189, 1127, 1016, 962, 820, 752, 702 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{18}NaO_2$ [M + Na]$^+$: 301.1199; found: 301.1203.

3-(4-(*Tert*-butyl)phenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ag). Colorless solid (78.7 mg, 82%), mp: 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 – 7.38 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.27 – 7.21 (m, 4H), 1.58 (s, 6H), 1.25 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 165.2, 151.4, 132.7, 129.0, 128.9, 128.7, 127.8, 126.6, 125.8, 125.0, 34.5, 31.1, 25.2. IR (KBr): 2955, 2845, 1741, 1509, 1456, 1277, 1190, 1107, 1017, 968, 837, 751, 696 2982, 2935, 2840, 1750, 1607, 1458, 1287, 1252, 1132, 965, 890, 837, 757, 702 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{22}H_{25}O_2$ [M + H]$^+$: 321.1849; found: 321.1846.

3-(4-Methoxyphenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ah).[15] Yellow solid (69.7 mg, 79%), mp: 88–90 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.36 (m, 3H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.23 – 7.19 (m, 2H), 6.74 (d, *J* = 7.6 Hz, 2H), 3.73 (s, 3H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 164.3, 159.5, 132.8, 130.4, 128.9, 127.8, 125.4, 122.0, 113.5, 85.6, 55.1, 25.3. IR (KBr): 2982, 2935, 2840, 1750,

1607, 1458, 1287, 1252, 1132, 965, 890, 837, 757, 702 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{18}NaO_3$ $[M + Na]^+$: 317.1148; found: 317.1152.

5,5-Dimethyl-4-phenyl-3-(4-(trifluoromethyl)phenyl)furan-2(*5H*)-one (3ai). White solid (81.7 mg, 82%), mp: 89–91 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.49 (q, *J* = 8.0 Hz, 4H), 7.45 – 7.38 (m, 3H), 7.20 (d, *J* = 4.80 Hz, 2H), 1.61 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 168.0, 133.3, 131.9, 130.2 (q, *J* = 32.5 Hz), 129.5, 129.3 (d, *J* = 26.0 Hz), 127.6, 125.1 (d. *J* = 1.8 Hz), 125.0 (d, *J* = 3.8 Hz), 124.9, 123.9 (d, *J* = 270.5 Hz), 86.1, 25.1. IR (KBr): 3062, 2986, 2936, 2872, 1753, 1492, 1325, 1282, 1121, 1068, 1016, 964, 890, 850, 757, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{15}F_3NaO_2$ $[M + Na]^+$: 355.0916; found: 355.0922.

5,5-Dimethyl-3-(4-nitrophenyl)-4-phenylfuran-2(*5H*)-one (3aj). Brick red solid (46.4 mg, 50%), mp: 116–118 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.8 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.48 – 7.42 (m, 3H), 7.21 – 7.17 (m, 2H), 1.63 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 169.3, 147.4, 136.2, 131.6, 130.0, 129.8, 129.4, 127.5, 124.6, 123.3, 86.4, 25.1. IR (KBr): 2923, 2853, 1750, 1646, 1518, 1347, 1017, 964, 857, 756, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{15}NNaO_4$ $[M + Na]^+$: 332.0893; found: 332.0900.

3-(3-Methoxyphenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-ono (3ak). Yellow solid (77.6 mg, 88%), mp: 113–114 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 4.4 Hz, 3H), 7.25 – 7.18 (m, 2H), 7.13 (t, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.91 (s, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 3.59 (s, 3H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 166.2, 159.1, 132.5, 130.8, 129.0, 128.9, 127.7, 125.9, 121.5,

114.8, 113.9, 85.6, 54.9, 25.2. IR (KBr): 3063, 2981, 2934, 2837, 1750, 1598, 1460, 1244, 1127, 1018, 963, 890, 755, 697 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{18}NaO_3$ $[M + Na]^+$: 317.1148; found: 317.1152.

3-(2-Methoxyphenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3al). White solid (75.0 mg, 85%), mp: 113–115 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 – 7.15 (m, 4H), 7.15 – 7.07 (m, 3H), 6.81 (t, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 3.44 (s, 3H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 167.3, 157.1, 132.9, 131.0, 129.9, 128.8, 128.3, 127.3, 124.9, 120.4, 119.3, 111.1, 86.2, 55.1, 25.7. IR (KBr): 3067, 2981, 2929, 2841, 1751, 1645, 1492, 1459, 1278, 11247, 1108, 1013, 963, 794, 754, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{18}NaO_3$ $[M + Na]^+$: 317.1148; found: 317.1151.

3-(3,4-Dimethoxyphenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3am). White solid (69.0 mg, 71%), mp: 110–112 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 6.8 Hz, 3H), 7.21 (d, *J* = 7.2 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 1H), 6.82 (s, 1H), 6.72 (d, *J* = 8.4 Hz, 1H), 3.80 (s, 3H), 3.51 (s, 3H), 1.56 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 164.3, 149.0, 148.1, 133.0, 129.0, 128.9, 127.8, 125.2, 122.1, 121.9, 111.9, 110.6, 85.4, 55.6, 55.3, 25.1. IR (KBr): 3057, 2927, 2843, 1748, 1516, 1459, 1258, 1126, 1021, 856, 815, 755, 702 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{21}O_4$ $[M + H]^+$: 325.1434; found: 325.1432.

3-(3,5-Dimethoxyphenyl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3an). Yellow solid (71.9 mg, 74%), mp: 163–165 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 5.6 Hz, 3H), 7.25 – 7.17 (m, 2H), 6.57 (s, 2H), 6.34 (s, 1H), 3.58 (s, 6H), 1.59 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 166.4, 160.3, 132.6, 131.2, 129.1, 129.0, 127.7, 125.9, 106.9, 101.5, 85.5, 55.1, 25.2. IR (KBr): 2932, 2843, 1746, 1600, 1459, 1365, 1273, 1203, 1160, 1071, 1026, 844, 744, 696 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{20}NaO_4$ $[M + Na]^+$: 347.1254; found: 347.1259.

5,5-Dimethyl-4-phenyl-3-(3,4,5-trimethoxyphenyl)furan-2(*5H*)-one (3ao). Pale yellow solid (53.1 mg, 50%), mp: 177–179 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.32 (m, 3H), 7.20 – 7.14 (m, 2H), 6.64 (s, 2H), 3.72 (s, 3H), 3.52 (s, 6H), 1.52 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 165.5, 152.7, 138.2, 133.1, 129.1, 129.0, 127.8, 125.3, 124.8, 106.3, 85.5, 60.8, 55.7, 25.2. IR (KBr): 3059, 2925, 2847, 1744, 1636, 1581, 1512, 1460, 1361, 1276, 1127, 1000, 903, 726, 644 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{21}H_{22}NaO_5$ $[M + Na]^+$: 377.1359; found: 377.1364.

3-(Benzo[d][1,3]dioxol-5-yl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3ap). White solid (68.4 mg, 74%), mp: 138-140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 (s, 3H), 7.20 (d, *J* = 4.0 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.85 (s, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 5.87 (s, 2H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 164.8, 147.6, 147.3, 132.5, 129.1, 129.0, 127.7, 125.5, 123.5, 123.4, 109.3, 108.1, 101.0, 85.6, 25.2. IR (KBr): 3085, 3045, 2989, 2924, 1745, 1484, 1436, 1365, 1240, 1031, 967, 873, 754, 752, 696, 642 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{19}H_{16}NaO_4$ $[M + Na]^+$: 331.0941; found: 331.0945.

5,5-Dimethyl-3-(naphthalen-2-yl)-4-phenylfuran-2(*5H*)-one (3aq). Colorless solid (76.3 mg, 81%), mp: 133–135 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1H), 7.72 (t, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.43 – 7.35 (m, 5H), 7.28 (d, *J* = 8.4 Hz,

1H), 7.23 (d, J = 4.8 Hz, 2H), 1.62 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 166.2, 132.9, 132.8, 132.4, 129.2, 129.1, 128.9, 128.4, 127.8, 127.5, 127.4, 127.1, 126.5, 126.2, 126.0, 85.8, 25.3. IR (KBr): 3057, 2982, 2932, 1749, 1212, 1076, 1019, 791, 751, 700 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{22}H_{18}NaO_2$ $[M + Na]^+$: 337.1199; found: 337.1204.

5,5-Dimethyl-4-phenyl-3-(pyridin-2-yl)furan-2(*5H*)-one (3ar). Colorless solid (73.9 mg, 93%), mp: 149–151 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.42 (d, J = 4.4 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 4.8 Hz, 3H), 7.18 (d, J = 4.8 Hz, 2H), 7.13 – 7.07 (m, 1H), 1.59 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3, 169.3, 149.5, 149.4, 136.0, 131.9, 128.9, 128.4, 127.6, 126.1, 124.4, 122.8, 86.0, 25.1. IR (KBr): 3078, 2982, 2930, 1757, 1581, 1464, 1438, 1358, 1280, 1212, 1015, 807, 754, 703 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{17}H_{15N}NaO_2$ $[M + Na]^+$: 288.0995; found: 288.0999.

5,5-Dimethyl-4-phenyl-3-(thiophen-2-yl)furan-2(*5H*)-one (3as).[15] Colorless solid (70.5 mg, 87%), mp: 154–156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, J = 5.2 Hz, 4H), 7.25 (d, J = 5.2 Hz, 2H), 7.20 (d, J = 4.8 Hz, 1H), 6.91 (t, J = 4.8 Hz, 1H), 1.55 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 162.2, 132.2, 131.3, 129.4, 129.3, 128.2, 127.6, 127.3, 126.7, 120.7, 86.0, 24.9. IR (KBr): 3100, 2982, 2927, 1746, 1440, 1361, 1279, 1231, 1118, 1052, 1005, 742, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{16}H_{14}NaO_2S$ $[M + Na]^+$: 293.0607; found: 293.0610.

3-(Benzo[b]thiophen-3-yl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3at). White solid (67.2 mg, 70%), mp: 141–143 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, J =

8.0 Hz, 1H), 7.54 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H), 7.25 – 7.18 (m, 6H), 7.11 (t, J = 7.6 Hz, 1H), 1.71 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 166.8, 139.8, 136.6, 131.9, 129.6, 128.8, 128.7, 127.8, 125.5, 124.3, 123.9, 123.0, 122.5, 122.2, 86.5, 26.1. IR (KBr): 3062, 2981, 2929, 2856, 1750, 1274, 1186, 1056, 1007, 729, 649 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{16}NaO_2S$ $[M + Na]^+$: 343.0763; found: 343.0766.

3-(Benzofuran-2-yl)-5,5-dimethyl-4-phenylfuran-2(*5H*)-one (3au). White solid (51.1 mg, 56%), mp: 143–145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (s, 1H), 7.52 – 7.29 (m, 6H), 7.18 (t, J = 7.6 Hz, 1H), 6.90 (t, J = 7.6 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 1.68 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.9, 164.2, 155.0, 146.6, 132.5, 129.6, 128.9, 128.0, 124.8, 124.3, 122.5, 121.7, 119.2, 111.3, 110.9, 86.7, 25.8. IR (KBr): 2982, 2927, 2854, 1750, 1649, 1451, 1255, 1114, 1077, 942, 749, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{16}NaO_3$ $[M + Na]^+$: 327.0992; found: 327.0996.

4-(4-(2-Hydroxyethoxy)phenyl)-5,5-dimethyl-3-phenylfuran-2(*5H*)-one (3ba). Pale yellow oil (66.1 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (dd, J = 6.8, 3.2 Hz, 2H), 7.25 (dd, J = 6.0, 3.2 Hz, 3H), 7.16 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 4.12 – 4.06 (m, 2H), 4.01 – 3.93 (m, 2H), 1.61 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 165.8, 159.3, 130.0, 129.5, 129.2, 128.3, 128.2, 125.8, 124.7, 115.0, 85.8, 69.2, 61.3, 25.5. IR (KBr): 3060, 2981, 2934, 2875, 1746, 1572, 1512, 1453, 1354, 1285, 1251, 1079, 1043, 964, 891, 799, 752, 697 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{20}NaO_4$ $[M + Na]^+$: 347.1254; found: 347.1257.

3,4-Diphenyl-1-oxaspiro[4.4]non-3-en-2-one (3ca).[5e] White solid (55.7 mg, 64%); mp: 154–156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (br, 5H), 7.24 – 7.18 (m, 5H), 2.14 – 1.95 (m, 5H), 1.75 (br, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 163.2, 132.5, 129.8, 129.1, 129.0, 128.9, 128.3, 128.2, 128.1, 127.3, 96.1, 36.2, 24.5. IR (KBr): 3022, 2959, 2926, 2876, 2851, 1743, 1440, 1355, 1156, 1124, 1073, 922, 798, 698, 640 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{18}NaO_2$ $[M + Na]^+$: 313.1199; found: 313.1202.

3,4-Diphenyl-1-oxaspiro[4.5]dec-3-en-2-one (3da).[5c] White solid (56.5 mg, 62%), mp: 182–184 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.34 (m, 5H), 7.23 – 7.14 (m, 5H), 1.89 – 1.69 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.5, 166.8, 132.8, 129.7, 129.1, 128.8, 128.3, 128.0, 127.9, 126.5, 87.4, 33.6, 24.4, 22.0. IR (KBr): 3071, 2938, 2857, 1741, 1560, 1493, 1445, 1352, 1274, 1186, 1121, 982, 764, 704, 643 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{21}H_{20}NaO_2$ $[M + Na]^+$: 327.1356; found: 327.1359.

5,5-Dimethyl-3-phenyl-4-(pyridin-2-yl)furan-2(*5H*)-one (3ea). White solid (63.6 mg, 80%), mp: 114–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.71 (d, J = 4.4 Hz, 1H), 7.52 (td, J = 7.6, 1.6 Hz, 1H), 7.41 – 7.35 (m, 2H), 7.36 – 7.31 (m, 3H), 7.28 – 7.22 (m, 1H), 7.13 (d, J = 7.6 Hz, 1H), 1.77 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3, 163.0, 151.3, 149.7, 136.1, 130.0, 129.3, 128.8, 128.5, 127.8, 125.2, 123.7, 86.7, 25.9. IR (KBr): 3058, 2980, 2931, 2859, 1749, 1580, 1460, 1356, 1286, 1212, 1131, 1097, 1015, 967, 922, 889, 749, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{17}H_{15}NNaO_2$ $[M + Na]^+$: 288.0995; found: 288.0998.

4,5,5-Trimethyl-3-phenylfuran-2(*5H*)-one (3fa). White solid (38.2 mg, 63%), mp: 94–96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 – 7.39 (m, 4H), 7.35 (t, J = 7.2 Hz, 1H), 2.12 (s, 3H), 1.52 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.5, 165.0, 130.2, 128.9, 128.4, 128.3, 125.6, 85.3, 24.7, 12.0. IR (KBr): 3058, 2981, 2927, 2855, 1748, 1664, 1442, 1381, 1292, 1221, 1166, 1081, 981, 937, 793, 751, 698, 635 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{13}H_{14}NaO_2$ $[M + Na]^+$: 225.0886; found: 225.0889.

5-Ethyl-4,5-dimethyl-3-phenylfuran-2(*5H*)-one (3ga). White solid (38.2 mg, 73%), mp: 68–70 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 – 7.40 (m, 4H), 7.39 – 7.34 (m, 1H), 2.07 (s, 3H), 2.02 – 1.92 (m, 1H), 1.80 – 1.71 (m, 1H), 1.51 (s, 3H), 0.84 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 163.6, 130.2, 129.0, 128.4, 128.3, 127.0, 87.7, 30.1, 23.5, 12.1, 7.4. IR (KBr): 3182, 3149, 2927, 2853, 1728, 1582, 1149, 756, 648 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{14}H_{16}NaO_2$ $[M + Na]^+$: 239.1043; found: 239.1044.

5-Isobutyl-4,5-dimethyl-3-phenylfuran-2(*5H*)-one (3ha). Colorless oil (29.3 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 – 7.40 (m, 4H), 7.37 (d, J = 6.0 Hz, 1H), 2.10 (s, 3H), 1.88 (d, J = 10.0 Hz, 1H), 1.62 (d, J = 11.2 Hz, 2H), 1.49 (s, 3H), 0.94 (dd, J = 12.0, 5.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.8, 164.4, 130.3, 128.9, 128.4, 128.3, 126.6, 45.6, 24.6, 24.3, 24.1, 23.9, 12.5. IR (KBr): 2957, 2926, 2873, 1750, 1590, 1459, 1382, 1307, 1206, 934, 793, 749, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{16}H_{20}NaO_2$ $[M + Na]^+$: 267.1356; found: 267.1357.

5-Hexyl-4,5-dimethyl-3-phenylfuran-2(*5H*)-one (3ia). White solid (40.8 mg, 50%), mp: 54–56 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 – 7.40 (m, 4H), 7.38 – 7.34 (m,

1H), 2.08 (s, 3H), 1.95 – 1.86 (m, 1H), 1.74 – 1.65 (m, 1H), 1.50 (s, 3H), 1.32 – 1.06 (m, 8H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.9, 164.0, 130.3, 129.0, 128.4, 128.3, 126.7, 87.5, 37.2, 31.6, 29.2, 23.8, 22.9, 22.5, 14.0, 12.2. IR (KBr): 3058, 2927, 2857, 1749, 1663, 1454, 1379, 1216, 1171, 980, 793, 750, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{24}NaO_2$ $[M + Na]^+$: 295.1669; found: 295.1673.

4,5-Dimethyl-3,5-diphenylfuran-2(*5H*)-one (3ja). Colorless oil (57.8 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, J = 7.6 Hz, 2H), 7.48 – 7.35 (m, 8H), 2.00 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2, 165.0, 138.4, 130.0, 129.0 128.8, 128.5, 128.4, 125.4(2), 125.3(5), 87.6, 22.9, 12.4. IR (KBr): 3060, 2989, 1752, 1573, 1446, 1380, 1128, 1066, 1026, 918, 792, 749, 697, 665 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{18}H_{16}NaO_2$ $[M + Na]^+$: 287.1043; found: 287.1047.

3,7a-Diphenyl-5,6,7,7a-tetrahydrobenzofuran-2(*4H*)-one (3ka). White solid (66.1 mg, 76%), mp: 98–100 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.6 Hz, 2H), 7.43 – 7.32 (m, 6H), 3.18 (t, J = 14.0 Hz, 2H), 2.38 – 2.22 (m, 1H), 2.03 – 1.86 (m, 2H), 1.80 (td, J = 13.2, 3.6 Hz, 1H), 1.59 – 1.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.6, 166.3, 136.7, 129.9, 129.0, 128.9, 128.5(0), 128.4(6), 126.9, 125.4, 86.6, 37.7, 27.6, 26.7, 22.4. IR (KBr): 3059, 2944, 2863, 1748, 1598, 1495, 1449, 1179, 1020, 984, 944, 789, 749, 696 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{18}NaO_2$ $[M + Na]^+$: 313.1199; found: 313.1202.

General procedure for preparation of oxazoles 4. To a 25 mL dried Schlenk tube was added the mixture of NaOH (0.6 mmol), CuI (0.03 mmol), secondary α-hydroxy ketones **1** (0.3 mmol), nitriles **2** (0.6 mmol), MeOH (1 mL) successively. The mixture

was then stirred at 80 °C for 24 h under N_2 atomsphere. After the reaction was completed, the mixture was cooled to room temperature and diluted with saturated brine water (15 mL), and extracted with EtOAc (10 mL×3). The organic phase was washed with H_2O (10 mL×3), dried over anhydrous Na_2SO_4, and then filtered. After removing the solvent under vacuum, the crude product was purified by column chromatography on a silica gel column using petroleum ether/ethyl acetate (30:1 to 4:1) as eluent to give the desired product **4**.

2-Benzyl-4,5-diphenyloxazole (4ma).[16] White solid (70.0 mg, 75%), mp: 85–87 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 – 7.69 (m, 2H), 7.64 – 7.58 (m, 2H), 7.46 (d, J = 7.2 Hz, 2H), 7.43 – 7.29 (m, 9H), 4.25 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.5, 145.6, 135.4, 135.2, 132.4, 128.9, 128.8, 128.6, 128.5(0), 128.4(6), 128.3, 128.0, 127.9, 127.0, 126.4, 34.7. IR (KBr): 3061, 3031, 2925, 2855, 1570, 1497, 1448, 1369, 1219, 1061, 1025, 988, 962, 765, 731, 695 cm^{-1}.

2-(4-Fluorobenzyl)-4,5-diphenyloxazole (4mb). White solid (79.9 mg, 81%), mp: 110–112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.2 Hz, 2H), 7.40 – 7.27 (m, 8H), 7.02 (t, J = 8.4 Hz, 2H), 4.15 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9 (d, J = 243.9 Hz), 161.3, 145.7, 135.2, 132.3, 131.1 (d, J = 3.3 Hz), 130.4 (d, J = 8.0 Hz), 128.8, 128.5 (d, J = 5.9 Hz), 128.4, 128.1, 127.9, 126.4, 115.5 (d, J = 21.3 Hz), 33.9. IR (KBr): 3059, 2927, 1601, 1572, 1509, 1445, 1158, 1096, 1060, 989, 915, 841, 763, 695 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{22}H_{17}FNO$ $[M + H]^+$: 330.1289; found: 330.1286.

2-(4-Chlorobenzyl)-4,5-diphenyloxazole (4mc). Pale yellow solid (89.0 mg, 86%), mp: 75–77 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 7.6 Hz, 2H), 7.41 – 7.29 (m, 10H), 4.18 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 145.8, 135.2, 133.9, 133.0, 132.3, 130.2, 128.8(3), 128.7(9), 128.6, 128.5(4), 128.5(0), 128.1, 127.9, 126.5, 34.1. IR (KBr): 3058, 2925, 2857, 1581, 1493, 1444, 1218, 1091, 1016, 772, 696 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{22}H_{16}ClNNaO$ [M + Na]$^+$: 368.0813; found: 368.0811.

2-(4-Bromobenzyl)-4,5-diphenyloxazole (4md). Yellow oil (81.7 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.2 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.39 – 7.23 (m, 8H), 4.14 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.9, 145.8, 135.2, 134.4, 132.3, 131.8, 130.6, 128.8, 128.6, 128.5(3), 128.4(9), 128.1, 127.9, 126.5, 121.1, 34.1. IR (KBr): 3057, 2926, 1569, 1488, 1445, 1368, 1218, 1013, 961, 914, 844, 763, 693 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{22}H_{16}BrNNaO$ [M + Na]$^+$: 412.0307; found: 412.0307.

2-(4-Iodobenzyl)-4,5-diphenyloxazole (4me). Yellow oil (73.4 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (t, J = 8.4 Hz, 4H), 7.59 – 7.54 (m, 2H), 7.41 – 7.31 (m, 6H), 7.17 (d, J = 8.0 Hz, 2H), 4.15 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.9, 145.8, 137.7, 135.3, 135.0, 132.3, 130.9, 128.8, 128.6, 128.5(1), 128.4(8), 128.1, 127.9, 126.5, 92.5, 34.2. IR (KBr): 3058, 2925, 1585, 1488, 1445, 1217, 1063, 1007, 772, 699 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{22}H_{17}INO$ [M + H]$^+$: 438.0349; found: 438.0351.

2-(4-Methylbenzyl)-4,5-diphenyloxazole (4mf). Yellow oil (89.7 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 7.6 Hz, 2H), 7.38 – 7.26 (m, 8H), 7.14 (d, J = 7.6 Hz, 2H), 4.15 (s, 2H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.8, 145.6, 136.6, 135.2, 132.5, 132.4, 129.4, 129.0, 128.7, 128.5(2), 128.4(8) 128.3, 128.0, 127.9, 126.4, 34.3, 21.0. IR (KBr): 3061, 2924, 1577, 1444, 1373, 1271, 1219, 1062, 979, 915, 769, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{20}NO$ $[M + H]^+$: 326.1539; found: 326.1540.

2-(4-Methoxybenzyl)-4,5-diphenyloxazole (4mh). White solid (85.9 mg, 84%), mp: 86–88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, J = 7.6 Hz, 2H), 7.56 (d, J = 7.6 Hz, 2H), 7.41 – 7.29 (m, 8H), 6.90 (d, J = 8.4 Hz, 2H), 4.16 (s, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.0, 158.6, 145.6, 135.1, 132.4, 129.9, 128.9, 128.6, 128.5, 128.4, 128.0, 127.9, 127.4, 126.4, 114.1, 55.2, 33.8. IR (KBr): 3056, 2929, 2839, 1603, 1509, 1449, 1249, 1175, 1034, 915, 834, 770, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{20}NO_2$ $[M + H]^+$: 342.1489; found: 342.1486.

4,5-Diphenyl-2-(4-(trifluoromethyl)benzyl)oxazole (4mi). Yellow solid (68.4 mg, 69%), mp: 102–104 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.56 (dd, J = 12.0, 8.0 Hz, 4H), 7.41 – 7.32 (m, 6H), 4.28 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 146.0, 139.4 (d, J = 1.2 Hz), 135.3, 132.2, 129.5 (d, J = 32.4 Hz), 129.2, 128.7, 128.6(2), 128.5(6), 128.2, 127.9, 126.5, 125.7 (q, J = 3.7 Hz), 124.1 (d, J = 270.3 Hz), 34.5. IR (KBr): 3063, 2927, 1585, 1499, 1443, 1325, 1167, 1123, 1066, 1019, 766, 696 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{17}F_3NO$ $[M + H]^+$: 380.1257; found: 380.1258.

2-(3-Methoxybenzyl)-4,5-diphenyloxazole (4mk). Yellow oil (69.6 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.6 Hz, 2H), 7.55 (d, J = 7.6 Hz, 2H), 7.38 – 7.23 (m, 7H), 7.02 – 6.93 (m, 2H), 6.81 (d, J = 8.4 Hz, 1H), 4.17 (s, 2H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.4, 159.8, 145.7, 136.9, 135.2, 132.4, 129.7, 128.9, 128.5(4), 128.4(9), 128.4, 128.0, 127.9, 126.4, 121.2, 114.6, 112.4, 55.2, 34.7. IR (KBr): 3057, 2937, 2839, 1594, 1490, 1448, 1262, 1158, 1049, 985, 872, 767, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{20}NO_2$ $[M + H]^+$: 342.1489; found: 342.1487.

2-(2-Methoxybenzyl)-4,5-diphenyloxazole (4ml). White solid (56.3 mg, 55%), mp: 49–51 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.6 Hz, 2H), 7.37 – 7.22 (m, 8H), 6.91 (dd, J = 16, 8.0 Hz, 2H), 4.22 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.9, 157.2, 145.3, 135.2, 132.6, 130.2, 129.1, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 126.4, 124.1, 120.5, 110.5, 55.5, 28.7. IR (KBr): 3058, 2934, 2841, 1588, 1494, 1453, 1246, 1174, 1113, 1043, 975, 914, 761, 678 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{23}H_{20}NO_2$ $[M + H]^+$: 342.1489; found: 342.1492.

4,5-Diphenyl-2-(3,4,5-trimethoxybenzyl)oxazole (4mo). White solid (69.6 mg, 71%), mp: 109–111 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, J = 7.6 Hz, 2H), 7.56 (d, J = 7.6 Hz, 2H), 7.40 – 7.28 (m, 6H), 6.65 (s, 2H), 4.13 (s, 2H), 3.87 (s, 6H), 3.84 (d, J = 0.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.5, 153.3, 145.7, 137.1, 135.2, 132.4, 131.0, 128.9, 128.6, 128.5(2), 128.4(5), 128.1, 127.9, 126.4, 106.0, 60.8, 56.1, 35.0. IR (KBr): 3066, 2928, 1581, 1503, 1455, 1328, 1234, 1121, 1005, 845,

767, 692 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{25}H_{24}NO_4$ $[M + H]^+$: 402.1700; found: 402.1702.

4,5-Diphenyl-2-(thiophen-2-ylmethyl)oxazole (4ms). Black solid (30.4 mg, 32%), mp: 65–67 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 6.8 Hz, 1H), 7.58 (d, *J* = 6.4 Hz, 1H), 7.39 – 7.30 (m, 3H), 7.23 (d, *J* = 4.8 Hz, 1H), 7.05 (d, *J* = 2.8 Hz, 1H), 6.98 (dd, *J* = 4.8, 3.6 Hz, 1H), 4.41 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 145.8, 136.9, 135.3, 132.3, 128.9, 128.6, 128.5(4), 128.5(2), 128.1, 127.9, 127.0, 126.5(3), 126.5(0), 124.9, 29.1. IR (KBr): 3059, 2922, 2856, 1577, 1449, 1222, 1051, 908, 838, 761, 689 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{16}NOS$ $[M + H]^+$: 318.0947; found: 318.0951.

2-(Benzofuran-3-ylmethyl)-4,5-diphenyloxazole (4mu). Yellow oil (76.9 mg, 73%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 6.4 Hz, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.38 – 7.23 (m, 8H), 4.25 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 155.3, 145.7, 142.6, 135.2, 132.3, 128.8, 128.6, 128.5(1), 128.4(6), 128.1, 127.9, 127.5, 126.4, 124.5, 122.6, 119.7, 114.4, 111.5, 23.4. IR (KBr): 3058, 2934, 2841, 1588, 1494, 1453, 1246, 1174, 1113, 1044, 975, 914, 761, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{18}NO_2$ $[M + H]^+$: 352.1332; found: 352.1336.

2-Benzhydryl-4,5-diphenyloxazole (4mw).[17] Pale yellow oil (110.3 mg, 95%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 7.6 Hz, 2H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 8.0 Hz, 4H), 7.35 – 7.20 (m, 12H), 5.71 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.9, 145.7, 139.8, 135.2, 132.4, 128.9, 128.7, 128.6, 128.5, 128.4(4), 128.4(0),

128.0, 127.9, 127.1, 126.5, 51.1. IR (KBr): 3045, 2927, 1958, 1891, 1576, 1490, 1366, 1292, 1208, 1064, 980, 917, 850, 753 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{28}H_{22}NO$ [M + H]$^+$: 388.1696; found 388.1698.

2-(4-Bromophenyl)-4,5-diphenyloxazole (4mx).[8c] White solid (25.9 mg, 23%), mp: 151–153 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.45 – 7.34 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 145.8, 136.9, 132.3, 132.0, 128.7(4), 128.7(2), 128.6(5), 128.3, 128.1, 127.9, 126.6, 126.3, 124.8, IR (KBr): 3044, 2923, 1586, 1471, 1358, 1263, 1164, 1075, 1014, 902, 817, 764, 682 cm^{-1}.

2-Benzyl-4,5-di-p-tolyloxazole (4na). Yellow oil (83.4 mg, 82%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.28 – 7.22 (m, 1H), 7.14 (dd, *J* = 12.0, 8.0 Hz, 4H), 4.18 (s, 2H), 2.35 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2, 145.6, 138.3, 137.7, 135.6, 134.6, 129.6, 129.2(1), 129.1(6), 128.8, 128.7, 127.7, 127.0, 126.4, 126.2, 34.7, 21.3. IR (KBr): 3063, 3030, 2922, 2859, 2732, 1574, 1520, 1496, 1453, 1424, 1024, 963, 820, 728, 695 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{22}NO$ [M + H]$^+$: 340.1696; found: 340.1700.

2-Benzyl-4,5-bis(4-methoxyphenyl)oxazole (4oa). Yellow oil (103.5 mg, 93%). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.39 (d, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.27 – 7.21 (m, 1H), 6.86 (dd, *J* = 13.6, 8.4 Hz, 4H), 4.16 (s, 2H), 3.79 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.9, 159.5, 159.2, 144.9, 135.6, 133.7, 129.0, 128.8, 128.6, 127.9, 126.9, 125.0,

121.7, 114.0, 113.9, 55.2, 34.7. IR (KBr): 3052, 2942, 2839, 1590, 1508, 1453, 1246, 1169, 1032, 831, 725 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{22}NO_3$ $[M + H]^+$: 372.1594; found: 372.1591.

9,10-Dimethoxy-3,3-dimethylphenanthro[9,10-*c*]furan-1(3*H*)-one (5). To a −40 °C stirred solution of **3am** (0.3 mmol) and phenyliodine(III) bis(trifluoroacetate) (0.33 mmol) in CH_2Cl_2 (2 mL) was added BF_3•Et_2O (0.36 mmol). The reaction mixture was stirred at −40 °C for 4 h. After the reaction was completed, the solvent was removed under vacuum and the residue was purified by column chromatography on silica gel using a mixture of petroleum ether and ethyl acetate (v/v = 10:1) as the eluent to give the desired product **5** as an off-white solid (30.9 mg, 32%); mp: 264–266 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.70 – 8.65 (m, 2H), 8.06 – 8.01 (m, 2H), 7.80 (t, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H), 4.13 (d, *J* = 8.0 Hz, 6H), 1.95 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.4, 152.7, 150.7, 150.1, 133.3, 128.9, 126.3, 125.8, 125.4, 124.1, 123.8, 122.1, 118.0, 104.5, 103.5, 84.7, 56.2, 56.0, 27.2. IR (KBr): 2923, 2850, 1728, 1519, 1450, 1270, 1200, 1021, 869, 758 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{20}H_{19}O_4$ $[M + H]^+$: 323.1278; found: 323.1279.

3-([1,1'-Biphenyl]-4-yl)-5,5-dimethyl-4-phenylfuran-2(5*H*)-one (6). To a 25mL oven-dried Schlenk tube equipped with a magnetic stirring bar was added **3ae** (0.3 mmol), phenylboronic acid (0.36 mmol), $PdCl_2$ (0.015 mmol), PPh_3(0.03 mmol), K_2CO_3 (1.2 mmol) and THF/water (3 mL, v/v = 2:1). The Schlenk tube was then capped and purged with N_2, and the reaction mixture was heated to 85 °C for 4 h. Upon completion of the reaction, the reaction mixture was cooled down to room

temperature, diluted with H_2O (20 mL) and extracted with EtOAc (15 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4 and then filtered. After removing the solvent under vacuum, the residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (v/v = 10:1) as the eluent to give the desired product **6** as a white solid (82.6 mg, 81%); mp: 174–175 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.57 (d, J = 8.0 Hz, 2H), 7.55 – 7.48 (m, 4H), 7.47 – 7.38 (m, 5H), 7.35 (d, J = 7.6 Hz, 1H), 7.31 – 7.25 (m, 2H), 1.65 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 166.0, 140.9, 140.2, 132.4, 129.4, 129.1, 129.0, 128.6, 128.5, 127.7, 127.4, 126.8, 126.7, 125.6, 85.7, 25.19. IR (KBr): 2980, 2927, 1749, 1273, 1203, 1015, 755, 698 cm^{-1}. HRMS-ESI (*m/z*): calcd for $C_{24}H_{21}O_2$ $[M + H]^+$: 341.1536; found: 341.1538.

Supporting Information

^1H and ^{13}C NMR spectra of all synthesized compounds (PDF)

X-ray structure and crystallographic data for compound **3ad** (CIF)

ACKNOWLEDGMENTS

We thank the National Key Research and Development Program of China (2016YFA0602900), the National Natural Science Foundation of China (21572071 and 21420102003) and the Natural Science Foundation of Guangdong Province (2017A030313054) for financial support.

REFERENCES

(1) For selective molecules containing butenolide moiety, see: (a) Michel, K.; Büther, K.; Law, M. P.; Wagner, S.; Schober, O.; Hermann, S.; Schäfers, M.; Riemann, B.;

Höltke, C.; Kopka, K. Development and Evaluation of Endothelin-A Receptor (Radio)Ligands for Positron Emission Tomography. *J. Med. Chem*. **2011**, *54*, 939–948. (b) Zhang, J.; Zhu, R.; Li, L.; Wang, Y.; Zhou, J.; Qiao, Y.; Zhang, Z.; Lou, H. Scapairrins A–Q, Labdane-Type Diterpenoids from the Chinese Liverwort *Scapania irrigua* and Their Cytotoxic Activity. *J. Nat. Prod*. **2015**, *78*, 2087–2094. (c) Shi, Y-S.; Liu, Y-B.; Ma, S-G.; Li, Y.; Qu, J.; Li, L.; Yuan, S-P.; Hou, Q.; Li, Y-H.; Jiang, J-D.; Yu, S-S. Bioactive Sesquiterpenes and Lignans from the Fruits of *Xanthium sibiricum*. *J. Nat. Prod*. **2015**, *78*, 1526–1535. (d) Wang, W.; Kim, H.; Nam, S-J.; Rho, B. J.; Kang, H. Antibacterial Butenolides from the Korean Tunicate *Pseudodistoma antinboja*. *J. Nat. Prod*. **2012**, *75*, 2049–2054. (e) Centko R. M.; Ramón-García, S.; Taylor, T.; Patrick, B. O.; Thompson, C. J.; Miao, V. P.; Anderen, R. J. Ramariolides A–D, Antimycobacterial Butenolides Isolated from the Mushroom *Ramaria cystidiophora*. *J. Nat. Prod*. **2012**, *75*, 2178–2182.

(2) For selective molecules containing oxazole moiety, see: (a) Yang, W. S.; Shimada, K.; Delva, D.; Patel, M.; Ode, E.; Skouta, R.; Stockwell B. R. Identification of Simple Compounds with Microtubule-Binding Activity That Inhibit Cancer Cell Growth with High Potency. *ACS Med. Chem. Lett*. **2012**, *3*, 35–38. (b) Desroy, N.; Moreau, F.; Briet, S.; Fralliec, G. L.; Floquet, S.; Durant, L.; Vongsouthi, V.; Gerusz, V.; Denis, A.; Escaich, S. Towards Gram-Negative Antivirulence Drugs: New Inhibitors of HldE Kinase. *Bioorg. Med. Chem*. **2009**, *17*, 1276–1289. (c) Wilson, Z. E.; Fenner, S.; Ley, S. V. Total Syntheses of Linear Polythiazole/Oxazole Plantazolicin A and Its Biosynthetic Precursor Plantazolicin

B. *Angew. Chem. Int. Ed*. **2015**, *54*, 1284–1288. (d) Banzragchgarav, O.; Murata, T.; Odontuya, G.; Buyankhishig, B.; Suganuma, K.; Davaapurev, B.-O.; Inoue, N.; Batkhuu, J.; Sasaki, K. Trypanocidal Activity of 2,5-Diphenyloxazoles Isolated from the Roots of *Oxytropis lanata*. *J. Nat. Prod*. **2016**, *79*, 2933–2940. (e) Parrish, S. M.; Yoshida, W.; Yang, B.; Williams, P. G. Ulapualides C-E Isolated from a Hawaiian *Hexabranchus sanguineus* Egg Mass. *J. Nat. Prod*. **2017**, *80*, 726–730.

(3) For examples of using butenolides as substrates, see: (a) Yavorshyy, A.; Shvydkiv, O.; Hoffmann, N.; Nolan, K.; Oelgemöller, M. Parallel Microflow Photochemistry: Process Optimization, Scale-up, and Library Synthesis. *Org. Lett.* **2012**, *14*, 4342–4345. (b) Ryu, D. H.; Lee, T. W.; Corey, E. J. Broad-Spectrum Enantioselective Diels-Alder Catalysis by Chiral, Cationic Oxazaborolidines. *J. Am. Chem. Soc.* **2002**, *124*, 9992–9993. (c) Fournier, J.; Lozano, O.; Menozzi, C.; Arseniyadis, S.; Cossy, J. Palladium-Catalyzed Asymmetric Allylic Alkylation of Cyclic Dienol Carbonates: Efficient Route to Enantioenriched γ-Butenolides Bearing an All-Carbon α-Quaternary Stereogenic Center. *Angew. Chem. Int. Ed.* **2013**, *52*, 1257–1261.

(4) For examples of using oxazoles as substrates, see: (a) Rendler, S.; Plefka, O.; Karatas, B.; Auer, G.; Fröhlich, R.; Mück-Lichterfeld, C.; Grimme, S.; Oestreich, M. Stereoselective Alcohol Silylation by Dehydrogenative Si-O Coupling: Scope, Limitations, and Mechanism of the Cu-H-Catalyzed Non-Enzymatic Kinetic Resolution with Silicon-Stereogenic Silanes. *Chem. Eur. J.* **2008**, *14*, 11512–11528. (b) Vedejs, E.; Grissom, J. W. 4-Oxazoline Route to Stabilized

Azomethine Ylides. Controlled Reduction of Oxazolium Salts. *J. Am. Chem. Soc.* **1988**, *110*, 3238–3246. (c) Griesbeck, A. G.; Fiege, M.; Lex, J. Oxazole-Carbonyl Photocycloadditions: Selectivity Pattern and Synthetic Route to *Erythro* α-Amino, β-Hydroxy Ketones. *Chem. Commun.* **2000**, 589–590.

(5) (a) Alfonsi, M.; Arcadi, A.; Chiarini, M.; Marinelli, F. Sequential Rhodium-Catalyzed Stereo- and Regioselective Addition of Organoboron Derivatives to the Alkyl 4-Hydroxy-2-Alkynoates/Lactonizaction Reaction. *J. Org. Chem.* **2007**, *72*, 9510–9517. (b) Bassetti, M.; D'Annibale, A.; Fanfoni, A.; Minissi, F. Synthesis of α,β-Unsaturated 4,5-Disubstituted γ-Lactones via Ring-Closing Metathesis Catalyzed by the First-Generation Grubbs' Catalyst. *Org. Lett.* **2005**, *7*, 1805–1808. (c) Liu, Y.; Song, F.; Guo, S. Cleavage of a Carbon-Carbon Triple Bond via Gold-Catalyzed Cascade Cyclization/Oxidative Cleavage Reactions of (*Z*)-Enynols with Molecular Oxygen. *J. Am. Chem. Soc.* **2006**, *128*, 11332–11333. (d) Egi, M.; Ota, Y.; Nishimura, Y.; Shimizu, K.; Azechi, K.; Akai, S. Efficient Intramolecular Cyclizations of Phenoxyethynyl Diols into Multisubstituted α,β-Unsaturated Lactones. *Org. Lett.* **2013**, *15*, 4150–4153. (e) Song, F.; Liu, Y. A Facile Approach to Spirocyclic Butenolides through Cascade Cyclization/Oxidative Cleavage Reactions of (*Z*)-Enynols Catalyzed by Gold under Dioxygen Atmosphere. *J. Organomet. Chem.* **2009**, *694*, 502–509.

(6) (a) Zheng, Y.; Li, X.; Ren, C.; Zhang-Negrerie, D.; Du,Y.; Zhao, K. Synthesis of Oxazoles from Enamides via Phenyliodine Diacetate-Mediated Intramolecular Oxidative Cyclization. *J. Org. Chem.* **2012**, *77*, 10353–10361. (b) Cheung, C. W.;

Buchwald, S. L. Room Temperature Copper(II)-Catalyzed Oxidative Cyclization of Enamides to 2,5-Disubstituted Oxazoles via Vinylic C-H Functionalization. *J. Org. Chem.* **2012**, *77*, 7526–7537. (c) Samanta, S.; Donthiri, R. R.; Dinda, M.; Adimurthy, S. Iodine Catalysed Intramolecular C(sp^3)-H Functionalization: Synthesis of 2,5-Disubstituted Oxazoles from *N*-Arylethylamides. *RSC Adv.* **2015**, *5*, 66718–66722. (d) Gao, W.-C.; Hu, F.; Huo, Y.-M.; Chang, H.-H.; Li, X.; Wei, W.-L. I_2-Catalyzed C-O Bond Formation and Dehydrogenation: Facile Synthesis of Oxazolines and Oxazoles Controlled by Bases. *Org. Lett.* **2015**, *17*, 3914–3917.

(7) (a) Lee, D.; Newman, S. G.; Taylor, M. S. Boron-Catalyzed Direct Aldol Reactions of Pyruvic Acids. *Org. Lett.* **2009**, *11*, 5486–5489. (b) Matsuo, K.; Shindo, M. Cu(II)-Catalyzed Acylation by Thiol Esters Under Neutral Conditions: Tandem Acylation-Wittig Reaction Leading to a One-Pot Synthesis of Butenolides. *Org. Lett.* **2010**, *12*, 5346–5349. (c) Li, S.; Miao, B.; Yuan, W.; Ma, S. Carbometalation-Carboxylation of 2,3-Allenols with Carbon Dioxide: A Dramatic Effect of Halide Anion. *Org. Lett.* **2013**, *15*, 977–979. (d) Cheng, J.; Chen, P.; Liu, G. Palladium-Catalyzed Cascade Cyclization for the Construction of Spiro-*N*,*O*-Acetals. *Org. Chem. Front.* **2014**, *1*, 289–293. (e) Mao, W.; Zhu, C. Synergistic Acid-Promoted Synthesis of Highly Substituted Butenolides via the Annulation of Keto Acids and Tertiary Alcohols. *Org. Lett.* **2015**, *17*, 5710–5713. (f) Li, X.; Han, C.; Yao, H.; Lin, A. Organocatalyzed [3 + 2] Annulation of Cyclopropenones and β-Ketoesters: An Approach to Substituted Butenolides with a Quaternary Center. *Org. Lett.* **2017**, *19*, 778–781.

(8) (a) Jiang, H.; Huang, H.; Cao, H.; Qi, C. TBHP/I_2-Mediated Domino Oxidative Cyclization for One-Pot Synthesis of Polysubstituted Oxazoles. *Org. Lett.* **2010**, *12*, 5561–5563. (b) Davies, P. W.; Cremonesi, A.; Dumitrescu, L. Intermolecular and Selective Synthesis of 2,4,5-Trisubstituted Oxazoles by a Gold-Catalyzed Formal [3 + 2] Cycloaddition. *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935. (c) Li, X.; Huang, L.; Chen, H.; Wu, W.; Huang, H.; Jiang, H. Copper-Catalyzed Oxidative [2 + 2 + 1] Cycloaddition: Regioselective Synthesis of 1,3-Oxazoles from Internal Alkynes and Nitriles. *Chem. Sci.* **2012**, *3*, 3463–3467. (d) Xu, W.; Kloeckner, U.; Nachtsheim, B. J. Direct Synthesis of 2,5-Disubstituted Oxazoles through an Iodine-Catalyzed Decarboxylative Domino Reaction. *J. Org. Chem.* **2013**, *78*, 6065–6074. (e) Zheng, M.; Huang, L.; Huang, H.; Li, X.; Wu, W.; Jiang, H. Palladium-Catalyzed Sequential C-N/C-O Bond Formations: Synthesis of Oxazole Derivatives from Amides and Ketones. *Org. Lett.* **2014**, *16*, 5906–5909. (f) Fan,Y.-S.; Das, U.; Hsiao, M.-Y.; Liu, M.-H.; Lin, W. Chemoselective Intramolecular Wittig Reactions for the Synthesis of Oxazoles and Benzofurans. *J. Org. Chem.* **2014**, *79*, 11567–11582. (g) Zeng, T.-T.; Xuan, J.; Ding, W.; Wang, K.; Lu, L.-Q.; Xiao, W.-J. [3 + 2] Cycloaddition/Oxidative Aromatization Sequence via Photoredox Catalysis: One-Pot Synthesis of Oxazoles from 2*H*-Azirines and Aldehydes. *Org. Lett.* **2015**, *17*, 4070–4073. (h) Chatterjee, T.; Cho, J. Y.; Cho, E. J. Synthesis of Substituted Oxazoles by Visible-Light Photocatalysis. *J. Org. Chem.* **2016**, *81*, 6995–7000. (i) Reddy, R. J.; Ball-Jones, M. P.; Davies, P. W. Alkynyl Thioethers in Gold-Catalyzed Annulations To Form Oxazoles. *Angew.*

Chem. Int. Ed. **2017**, *56*, 13310–13313.

(9) (a) He, H.; Qi, C.; Hu, X.; Ouyang, L.; Xiong, W.; Jiang, H. Copper-Catalyzed [4 + 1] Annulation between α-Hydroxy Ketones and Nitriles: An Approach to Highly Substituted 3(2*H*)-Furanones. *J. Org. Chem.* **2015**, *80*, 4957–4965. (b) Qi, C.; Peng, Y.; Ouyang, L.; Ren, Y.; Jiang, H. Base-Promoted Addition of Arylacetonitriles to Terminal Alkynes: Regio- and Stereoselective Access to Disubstituted Acrylonitriles. *Adv. Synth. Catal.* **2017**, *359*, 1339–1350. (c) He, H.; Qi, C.; Ou, Y.; Xiong, W.; Hu, X.; Ren, Y.; Jiang, H. Base-Promoted Annulation of α-Hydroxy Ketones and Dimethyl But-2-ynedioate: Straightforward Access to Pyrano[4,3-*a*]quinolizine-1,4,6(2*H*)-triones and 2*H*-Pyran-2,5(6*H*)-diones. *Org. Biomol. Chem.* **2014**, *12*, 8128–8131.

(10) CCDC 1587650 contains the supplementary crystallographic data for compound 3ad. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

(11) For the review on the *gem*-substituent effect, see: Jung, M. E.; Piizzi, G. *gem*-Disubstituent Effect: Theoretical Basis and Synthetic Applications. *Chem. Rev.* **2005**, *105*, 1735–1766.

(12) Loo, A. A.; Holton, M. K.; Downey, C. R.; White, T. M.; Rolph, C. E.; Bruening, S. R.; Li, G.; Delaney, K. M.; Pelkey, S. J.; Pelkey, E. T. Preparation of Dibenzo[*e,g*]isoindol-1-ones via Scholl-Type Oxidative Cyclization Reactions. *J. Org. Chem*. **2014**, *79*, 8049–8058.

(13) (a) Liang, Y-F.; Jiao, N. Highly Efficient C-H Hydroxylation of Carbonyl

Compounds with Oxygen under Mild Conditions. *Angew. Chem. Int. Ed*. **2014**, *53*, 548–552. (b) Liang, Y.-F.; Wu, K.; Song, S.; Li, X.; Huang, X.; Jiao, N. I_2- or NBS-Catalyzed Highly Efficient α-Hydroxylation of Ketones with Dimethyl Sulfoxide. *Org. Lett*. **2015**, *17*, 876–879. (c) He, H.; Qi, C.; Hu, X.; Yuan, G.; Jiang, H. Efficient Synthesis of Tertiary α-Hydroxy Ketones through CO_2-Promoted Regioselective Hydration of Propargylic Alcohols. *Green Chem*. **2014**, *16*, 3729–3733.

(14) Ros, F.; Rosa, J.; Enfedaque, J. Alkylation of Nitrile Anions by Tertiary α-Halo Ketones and Nitriles. *J. Org. Chem*. **1995**, *60*, 5419–5424.

(15) Blagoev, B.; Novkova, S. Addition of Reactive Dimetallic Ambidents to the Azirine Double Bond. *Tetrahedron* **1982**, *38*, 1609–1613.

(16) Evans, D. A.; Nagorny, P.; Xu, R. Ceric Ammonium Nitrate Promoted Oxidation of Oxazoles. *Org. Lett*. **2006**, *8*, 5669–5671.

(17) Martín, R.; Cuenca, A.; Buchwald, S. L. Sequential Copper-Catalyzed Vinylation/Cyclization: An Efficient Synthesis of Functionalized Oxazoles. *Org. Lett*. **2007**, *9*, 5521–5524.