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Copper-Catalyzed Intramolecular Annulation of Conjugated Enynones to Substituted 1*H*-Indenes and Mechanistic Studies

Chao Pei,[†] Guang-Wei Rong,[†] Zhi-Xiang Yu,*[,‡] and Xin-Fang Xu*[,†,§]

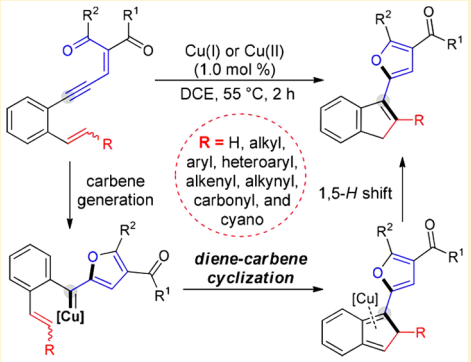
[†]Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, China

[‡]Beijing National Laboratory for Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China

[§]School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou 510006, China

Supporting Information

ABSTRACT: Herein, a copper-catalyzed intramolecular cascade reaction of conjugated enynones to deliver substituted 1*H*-indenes is reported. The inexpensive and less toxic copper salt served as the only catalyst in the transformation, affording the 3-(2-furyl)-substituted 1*H*-indenes in good to excellent yields under mild reaction conditions with broad functional group tolerance and making it highly appealing for synthetic organic chemistry. Notably, detailed DFT calculations have been carried out to elucidate that the reaction undergoes a copper-mediated 5-*exo*-*dig* cyclization of enynones to afford copper-(2-furyl)-carbene intermediate, followed by diene-carbene cyclization (one step but involving 6π cyclization of Cu-carbene and reductive elimination) and 1,5-hydrogen shift to provide the 1*H*-indenes.



INTRODUCTION

Metal carbene, which is commonly generated from the diazo compound, is one of the versatile intermediates in organic synthesis, and plays a critical role in the construction of complex molecules due to its versatile reactivity.[1] Particularly, metal carbene reactions show advantages in the direct C−C bond formation through various types of transformations, such as C−H insertion,[2] cross-coupling reaction,[3] cyclization reaction,[4] and others.[5] Among these advances, the vinylic C(sp^2)−H bond insertion to form C(sp^2)−C(sp^3) bonds remains much less developed, possibly because of the competing cyclopropanation reaction with electron-rich alkenes.[6] Recently, two formal vinylic C(sp^2)−H insertion reactions to form substituted 1*H*-indenes with *N*-tosylhydrazones were reported by Bruin's group and Wang's group via Co(III)-carbene radical and Rh(II)-carbene intermediates, respectively (Scheme 1a).[7] Meanwhile, our group has also disclosed a carbene/alkyne metathesis cascade reaction terminating in analogous vinyl carbene transfer procedure, which was commonly considered as [3 + 2] cycloaddition (Scheme 1b).[8]

On the other hand, transition-metal-catalyzed cyclization reactions of conjugated enynals or enynones through 5-*exo*-*dig* nucleophilic attack have become an efficient way to generate the furyl metal-carbene intermediate.[9] Many efforts have been endeavored to the development of effective catalytic transformations with this novel carbene precursor, including Cr,[10] Cu,[11] Au,[12] Rh,[13] Zn,[14] Pd,[15] and organocatalysis.[16] Recently, aromatic C(sp^2)−H bond insertion and C(sp^3)−H bond insertion reactions with in situ generated Zn(II) (2-furyl) carbene were reported by Vicent, López and co-workers.[14a] Moreover, the enantioselective intramolecular C(sp^3)−H bond insertion reaction to form new C−C bond catalyzed by chiral Rh(II) complexes has been reported by Zhu and co-workers.[13e] In addition, these conjugated enynones could also serve as safe and effective alternatives in Pd-catalyzed carbene coupling reactions according to Wang's work, providing a practical synthetic method for C—C and C═C bond formations.[15a,b] Encouraged by these works and as a continuation of our interest in the carbene cascade transformations,[15c,17] we were intrigued by the possibility that the conjugated enynone can act as carbene precursor for the formal vinylic C(sp^2)−H bond insertion reaction, thus realizing new C−C bond formation.

Considering that indenes are one of the most important structures pervasively existing in many natural products,[18] bioactive compounds[19] and metallocene complexes,[20] we decided to conduct the above vision for the synthesis of indenes by using **1** (Scheme 1c). During our experimental investigation, Wang's group reported similar vinylic C(sp^2)−H bond insertion reaction with hydrazone as carbene precursor.[7b] We found that **1** gave a formal coupling product **2** instead of C(sp^2)−H insertion product **2′**, which was the expected

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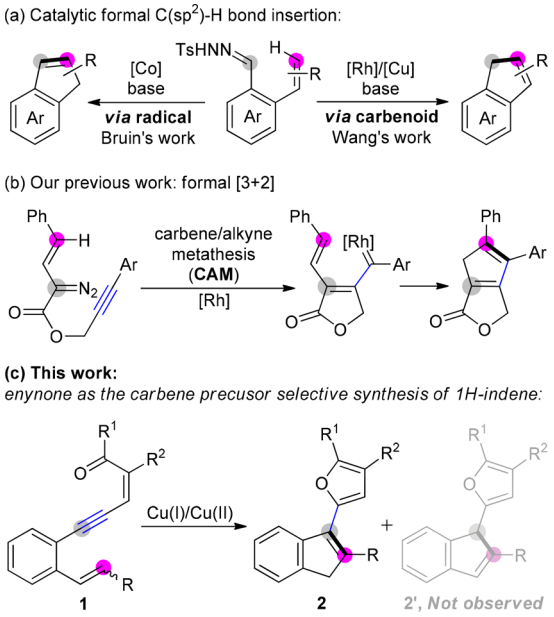
Scheme 1. Catalytic Carbon−Carbon Bond Formation of Metal Carbene



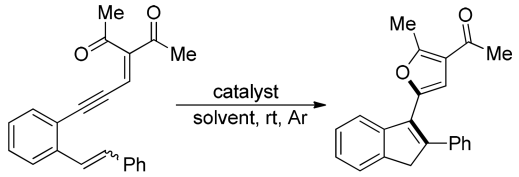
product based on Wang's work. We hypothesized that **2′** was first generated and then converted to **2** via 1,5-hydrogen shift (this hypothesis will be studied in the present work). Here we disclose our results of converting **1** to **2** with inexpensive and low toxic copper salt as catalyst under mild conditions, which serves as an efficient method to access 1*H*-indenes. Meanwhile, we carried out DFT study of the mechanism of our present reaction. These computational studies will not only help to understand the reaction mechanisms of the present reaction, but also provide some insights and guidances for future design of vinylic C−H bond insertion reactions.

RESULTS AND DISCUSSION

We began our study by using the styrene tethered enynone **1a** as the model substrate (*Z*: *E* ≈ 1:1). The 1*H*-indene **2a** was obtained in 95% isolated yield with $Rh_2(OAc)_4$ as the catalyst in 1,2-dichloroethane (DCE) at room temperature (Table 1, entry 1). In addition to $Rh_2(OAc)_4$, other catalysts, such as $Cu(OTf)_2$, $AuCl_3$, $(\eta^3\text{-}C_3H_5)_2Pd_2Cl_2$, CuI, CuCl, $CuCl_2$, and $CuSO_4{\cdot}5H_2O$, could also promote this annulation (entries 2−8). However, $ZnCl_2$, as the effective catalyst in other transformations with conjugated enynones, failed to catalyze this reaction (entry 9).[14] Notably, CuI or $CuSO_4{\cdot}5H_2O$ as a cheap and low toxic catalyst had an obvious advance (entries 5 and 8). To our delight, carrying out the reaction at higher temperature led to 100% conversion with 88%−95% isolated yields in the presence of corresponding copper salt (entries 10−12). Further investigation of solvents showed that >90% yields were obtained when the reaction was carried out in DCE, chloroform, or ethyl acetate (entries 12−14), thus demonstrating extraordinary robustness of this process. The molecular structure of **2a** was inferred from NMR spectra analysis of its analogue **2b** (see the Supporting Information).[13b]

Scope of the Reaction. With the optimized reaction conditions in hand, various enynones **1** were prepared to test the generality of this cyclization (Scheme 2). First, we investigated the influence of the aromatic substituent attached

Table 1. Condition Optimization[a]



1a, (*Z* : *E* = 1 : 1) **2a**

entry	solvent	catalyst	time	% yield (% conv)[b]
1	DCE	$Rh_2(OAc)_4$	20 min	95 (100)
2	DCE	$Cu(OTf)_2$	20 min	90 (100)
3	DCE	$AuCl_3$	20 min	75 (100)
4	DCE	$(\eta^3\text{-}C_3H_5)_2Pd_2Cl_2$	20 min	65 (100)
5	DCE	CuI	8 h	92 (100)
6	DCE	CuCl	16 h	56 (60)
7	DCE	$CuCl_2$	16 h	42 (50)
8	DCE	$CuSO_4{\cdot}5H_2O$	16 h	32 (35)
9	DCE	$ZnCl_2$	16 h	<5 (100)
10[c]	DCE	CuCl	2 h	90 (100)
11[c]	DCE	$CuCl_2$	2 h	88 (100)
12[c]	DCE	$CuSO_4{\cdot}5H_2O$	2 h	95 (100)
13[c]	$CHCl_3$	$CuSO_4{\cdot}5H_2O$	2 h	92 (100)
14[c]	EA	$CuSO_4{\cdot}5H_2O$	2 h	92 (100)
15[c]	PhMe	$CuSO_4{\cdot}5H_2O$	2 h	50 (55)
16[c]	EtOH	$CuSO_4{\cdot}5H_2O$	2 h	85 (100)

[a]Reaction conditions: the reaction was carried out on a 0.2 mmol scale, **1a** (62.8 mg, 0.2 mmol), and catalyst (1.0 mol %) at room temperature in corresponding solvent (2.0 mL) under argon atmosphere. [b]Isolated yields. [c]Reaction was performed at 55 °C. EA = ethyl acetate.

the vinylic double bond (R^3 = Ar). The substrates with electron-withdrawing or electron-donating groups in the *para*-position on the aromatic ring all gave the corresponding products in excellent yields (92−97%, Scheme 2, **2b**−**2g**). Pleasingly, the sterically encumbered substrates had only a slight effect on this transformation, and comparably high yields were obtained for *ortho*, *meta*-substituted and disubstituted enynones (Scheme 2, **2h**−**2k**). It was noted that the substrates bearing 1-naphthyl and 2-thienyl substituent produced the corresponding products **2l** and **2m** in 92% and 97% yields, respectively. In addition to the aryl group, R^3 could also be alkenyl (**1n**), alkynyl (**1o**), and alkyl (**1p** and **1q**) groups, and the corresponding products were isolated in 88−98% yields. In all these above cases (**1a**−**1q**), mixed material with both *Z*- and *E*-isomers was used, and both of these isomers were converted to the same 1*H*-indene product **2**. Notably, the terminal alkene tethered enynone **1r** also smoothly transformed to the product **2r** in 84% yield. Next, when changing the R^3 to electron-withdrawing ester group, the cinnamate-tethered enynone **1s**, which was prepared and isolated as a single *E*-configuration, performed well to offer the target product **2s** in 91% yield under these conditions. Two other benzoyl and *para*-chlorobenzoyl derivatives were also suitable for this transformation, although longer reaction time was needed (**2t** and **2u**). It was worth mentioning that for the enynone **1v**, which was prepared and isolated as a mixture of *Z*- and *E*-isomers, only the *E*-isomer worked in this reaction and delivered the corresponding product in 81% yield based on the used amount of the *E*-isomer, and with *Z*-**1v** recovered in 98% yield.[11d] Moreover, the *α*,*β*-unsaturated ketone and nitrile substrates **1w** and **1x** worked less effectively, producing the

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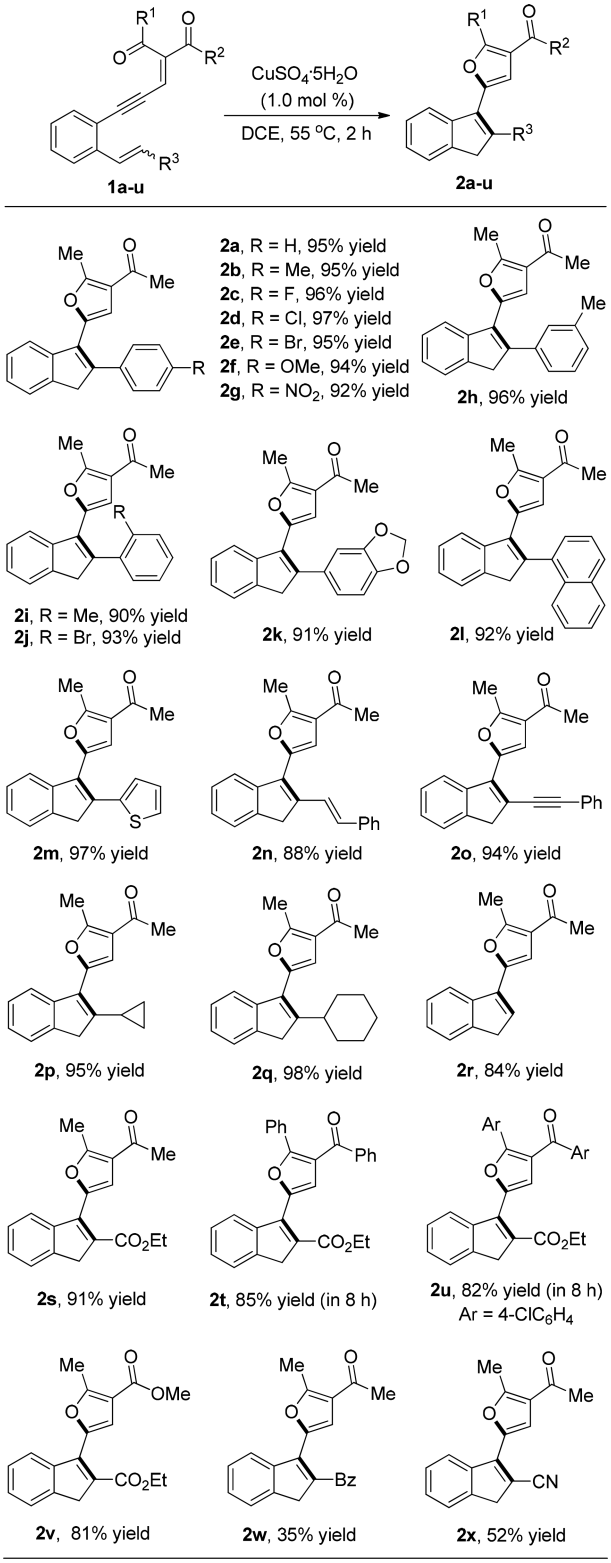
Scheme 2. Substrate Scope[a]

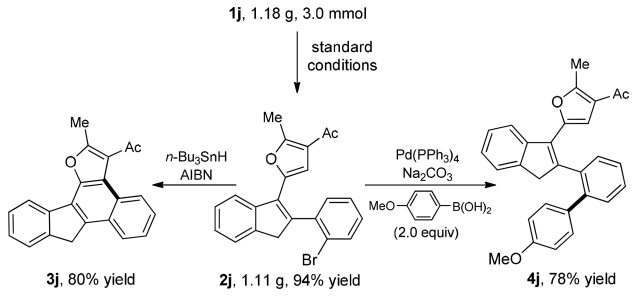


[a]Reaction conditions: **1** (0.20 mmol) and $CuSO_4·5H_2O$ (0.5 mg, 1.0 mol %) in DCE (2.0 mL) at 55 °C under argon atmosphere for 2 h, and the yields are given in isolated yields.

corresponding 1*H*-indenes in moderate yields (**2w** and **2x**), which may due to the lower nucleophilicity of these substrates.

Furthermore, this cascade cyclization reaction could be easily scaled up to gram scale, which afforded 1.11 g of product **2j** in 94% yield in the presence of 1.0 mol % copper catalyst (Scheme 3). Further transformations were carried out to

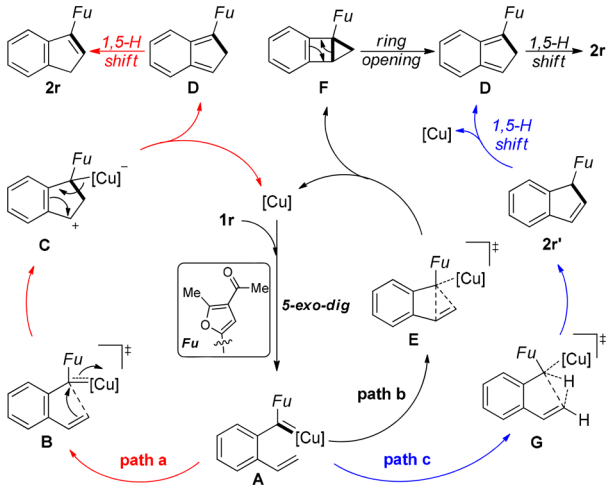
Scheme 3. Scale-Up and Derivatizations



demonstrate the utility of these products, including radical annulation and Suzuki coupling reaction of the bromo-derivative **2j** to give **3j** and **4j** in 80% and 78% yields, respectively.

Mechanistic Study. Scheme 4 depicts the proposed pathways of the present reaction. First, in the presence of

Scheme 4. Proposed Reaction Pathways



copper catalyst, enynone **1r** undergoes a 5-*exo-dig* cyclization to form Cu-carbene intermediate **A** via nucleophilic attack of carbonyl oxygen to internal carbon of alkyne. From Cu-carbene **A**, three possible pathways are possible for the formation of product **2r**. In *path a*, intramolecular nucleophilic attack of the vinylic double bond to the electron deficient carbene-carbon center of Cu-carbene **A** generates intermediate **C**. Then intermediate **C** releases copper catalyst to give isoindene intermediate **D**, which then gives product **2r** through a 1,5-hydrogen shift process.[7b] In *path b*, Cu-carbene **A** undergoes a cyclopropanation reaction to give cyclopropane intermediate **F**, which produces isoindene intermediate **D** via ring expansion. Intermediate **D** then undergoes a 1,5-hydrogen shift to afford product **2r**. In *path c*, a direct intramolecular C(sp^2)−H bond insertion of Cu carbene **A** occurs via transition state **G**. The corresponding insertion product **2r′** is then converted to the target molecular **2r** through two successive 1,5-hydrogen shifts.

To get more mechanistic information, several control experiments were carried out (Scheme 5). First, the reaction of trisubstituted olefin **1y** generated a mixture of **2y** and **2y′**,

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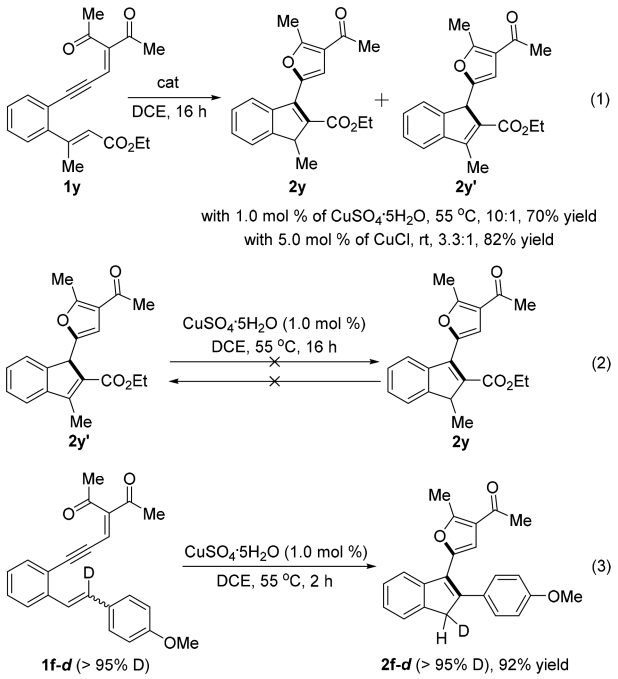
Scheme 5. Mechanistic Experiments



which were separated by column chromatography (eq 1). Further study showed that no interconversion of **2y′** and **2y** took place under the standard reaction conditions (eq 2). These results ruled out the possibility of the proposed concerted C(sp^2)−H bond insertion path way (*path c*). In addition, we have also performed deuterium labeling experiments, finding that this reaction has an intramolecular hydrogen transfer process instead of adopting the deprotonation/protonation process mentioned in previous report (eq 3).[7b]

We then performed DFT calculations at the B3LYP/6-311+G(d,p)(SDD)//B3LYP/6-31G(d)(SDD) level to differentiate the above-mentioned three pathways (same conclusions were found by using other DFT functionals such as B3LYP-D3,[21] see the Supporting Information). Experimentally both Cu(I) and Cu(II) salts, such as CuI, CuCl, $CuCl_2$ and $CuSO_4·5H_2O$, can catalyze the target reaction with high efficiency. However, we found that calculations using $CuSO_4·5H_2O$ were difficult to converge. Therefore, we concentrated our calculations using both $CuCl_2$ and CuCl. We present the potential energy surfaces for CuCl in the main text of this paper, while the potential energy surface for $CuCl_2$ is given in the Supporting Information. For simplification of the calculations, the terminal alkene substituted enynone **1r** was chosen as the model substrate. We discuss here all these pathways using the computed Gibbs free energy in solution, and the computed data in the gas phase were also given for reference in the potential energy surfaces.

As shown in Figure 1, our calculations indicate that the initial step of the coordination of CuCl with **1r** to form chelation complex **INT1** is a facile process and is exergonic by 7.0 kcal/mol. From copper complex **INT1**, the intramolecular ligand exchange to isomer **INT2** is endergonic by 4.0 kcal/mol. Then intermediate **INT2** undergoes another facile process, the 5-*exo*-*dig* cyclization via **TS2−3** with an activation free energy of 6.1 kcal/mol, which prefers a *trans*-addition of the carbonyl group and copper to the alkyne, giving the Cu-carbene intermediate **INT3**.[22] In Cu-carbene intermediate **INT3**, the copper−carbon bond has a length of 1.89 Å, which is slightly longer than the value obtained from experimental data for other Cu-carbene complexes (1.87−1.89 Å).[23]

For the followed transformation, first, we considered the intramolecular nucleophilic attack of the vinylic double bond from Cu carbene intermediate **INT3** in *path a*. The required free energy via transition state **TS3−4** in converting **INT3** to **INT4** is 9.9 kcal/mol, and this step is exergonic by 14.6 kcal/mol. This step can be understood by analogy to diene-carbene cyclization, which involves 6π cyclization and reductive elimination process (Figure 2). We computed a simple model system of dienyl carbene **INT6**, finding that it undergoes a facile 6π cyclization to give intermediate **INT7** via **TS6−7** with the activation free energy of 10.3 kcal/mol. Then the $\Delta G^{\ddagger}$ for reductive elimination to give the cyclopentadiene-CuCl complex **INT8** needs only 0.7 kcal/mol. However, in the present system for **INT3**, which is similar to **INT6** and more stable due to the additional aromatic ring, the IRC calculations showed that it does not go through cyclization process but directly gives the isoindene **INT4** through reductive elimination transition state (see the Supporting Information). Actually in **INT3**, the distance between vinyl carbon and copper is 2.84 Å, and in the **TS3−4**, this distance is reduced to 2.42 Å and the forming C−C bond is 2.06 Å. We reasoned that, for **INT3**, the 6π cyclization transition state, its intermediate, and the followed reductive elimination transition state, all are close in energy and only the reductive elimination transition state **TS3−4** can be located computationally.

Formation of isoindene intermediate **INT4** is irreversible because the followed step of 1,5-*H* shift is easier (see later discussion) than the backward reaction from **INT4** to **INT3**. Isoindene intermediate **INT4** can be converted to the more favorable intermediate **INT5** through an intramolecular ligand exchange, which is exergonic by 7.3 kcal/mol.[24] Then an intramolecular 1,5-hydrogen shift converts intermediate **INT5** to the indene-coordinated copper intermediate **2r-CuCl** irreversibly via a three-membered ring transition state **TS5−2r** with an energy barrier of 16.9 kcal/mol. An alternative pathway of 1,5-hydrogen shift via transition state **TS5−2r′** has also been considered. This step giving the isomer **2r′-CuCl** has an activation free energy of 20.4 kcal/mol, which is 3.5 kcal/mol higher than its competing process via **TS5−2r**. Therefore, 3-(2-furyl)-1*H*-indenes will be dominantly generated, with a predicted ratio of **2r**:**2r′** by 180:1 at 55 °C. This agrees with experimental results (this ratio was greater than 20:1, as determined by NMR experiments). The preference of 1,5-*H* shifts can be understood because the formation of **2r′** via **TS5−2r′** has to disrupt the conjugation between indene and furan, which is kept in **TS5−2r**. This can be appreciated by the structures of 1,5-*H* migration transition states **TS5−2r** and **TS5−2r′**, in which the coplanar structure was kept in transition state **TS5−2r** with dihedral angles of $C_1-C_2-C_3-O$ −8.57° and $C_1-C_2-C_3-C_4$ 177.30°. While the coplanarity was broken in the transition state **TS5−2r′** for the increase of dihedral angles of $C_1-C_2-C_3-O$ (33.77°) and $C_1-C_2-C_3-C_4$ (−166.05°), confirming the disruption of conjugation in the formation of **2r′** from **INT5** via **TS5−2r′**.

In the final step of the catalytic cycle, product **2r** is released via catalyst transfer between complex **2r-CuCl** and substrate **1r**, together with liberation of CuCl for the next catalytic cycle.

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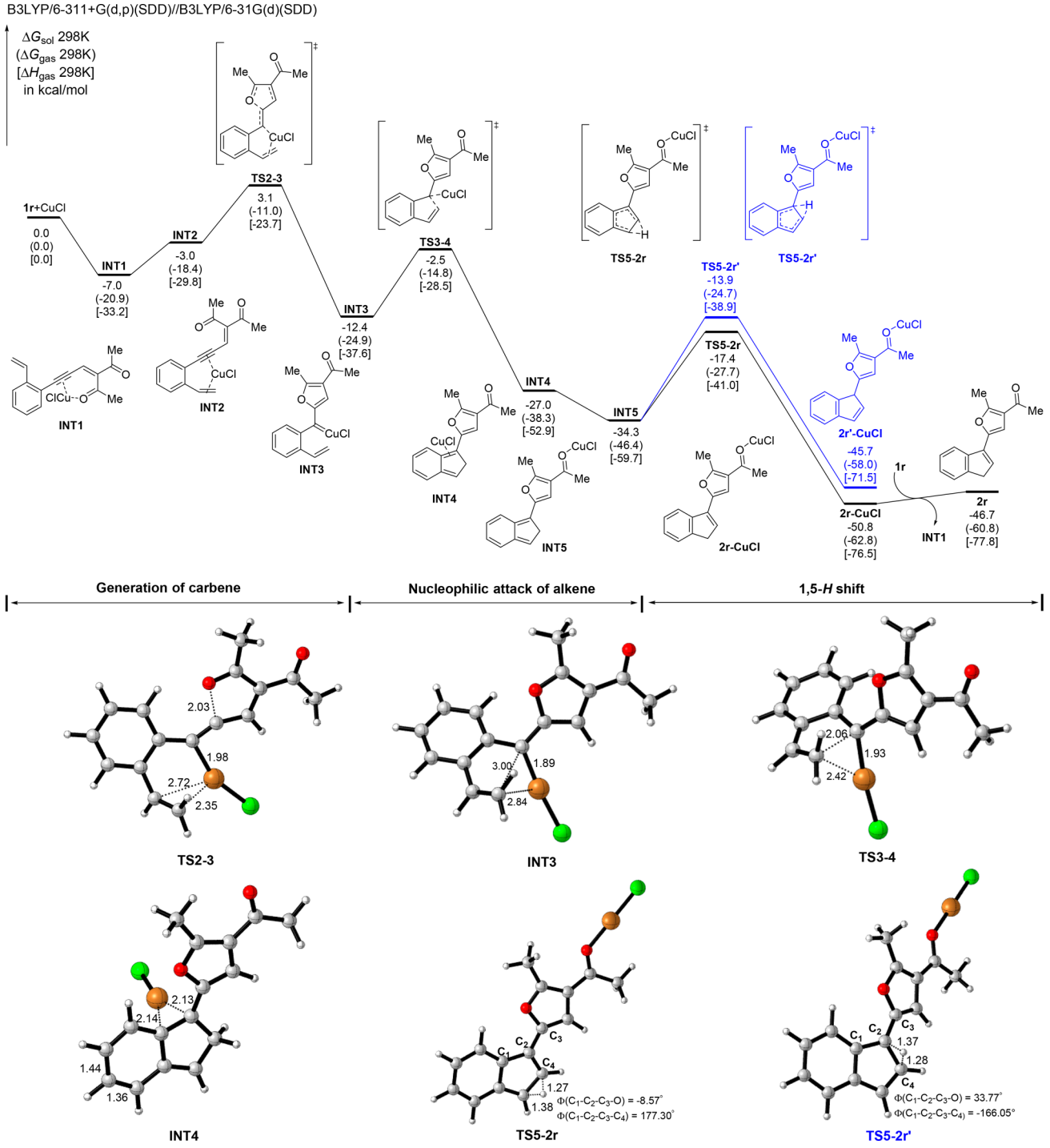

Figure 1. Potential energy surface and 3D structures of key species of CuCl-catalyzed cascade annulation of **1r**. The bond lengths in the structures at the bottom are given in Å.

Calculations indicated that this ligand exchange process is slightly endergonic by 4.1 kcal/mol.

The pathway for intramolecular cyclopropanation in *path b* is shown in Figure 3. The corresponding activation free energy of this cyclopropanation via transition state **TS3−9** is 30.4 kcal/mol, which is higher than the cyclization transition state **TS3−4** in *path a* by 20.5 kcal/mol. Generation of cyclopropanation intermediate **INT9** from **INT3** is endergonic by 24.8 kcal/mol. Therefore, *path b* is not favored compared to *path a*.

Furthermore, we tried to locate a concerted C(sp^2)−H bond insertion transition state from intermediate **INT3**, which was described in *path c*. However, all attempts in locating such a transition state led to the nucleophilic attack transition state in *path a*. Therefore, this pathway would not exist at this computational level. Overall, the experimental and calculation results unveil that the nucleophilic attack of the vinylic double bond and then 1,5-hydrgon shift in *path a* is the most favorable pathway to account for this transformation.

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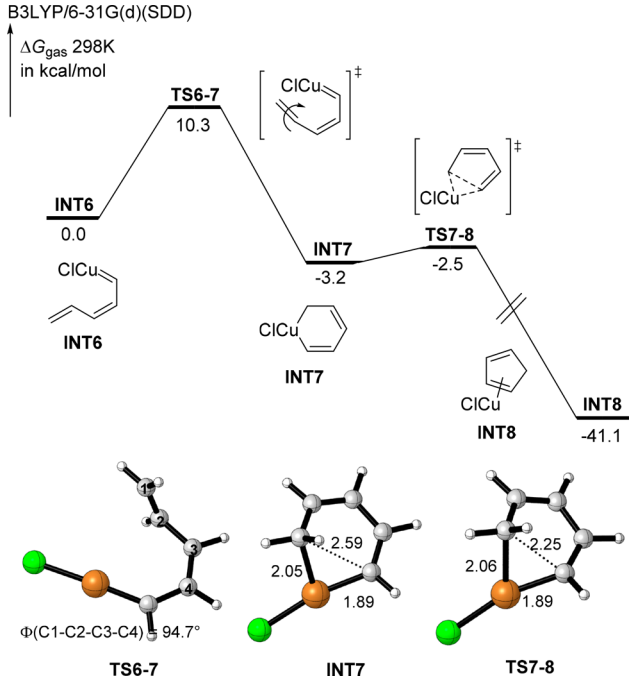

Figure 2. Potential energy surface and 3D structures of key species for the annulation of dienyl-carbene. The bond lengths in the structures at the bottom are given in Å.

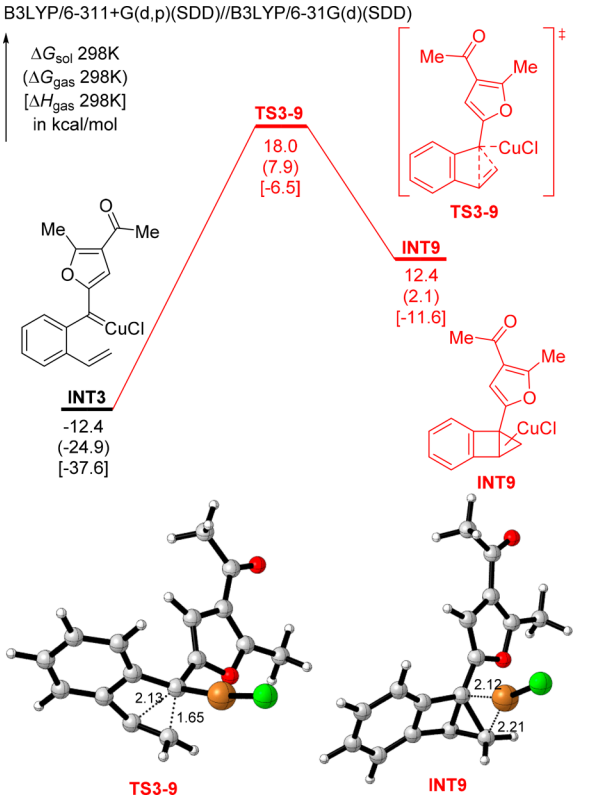

Figure 3. Potential energy surface and 3D structures of key species of intramolecular cyclopropanation. The bond lengths in the structures at the bottom are given in Å.

CONCLUSIONS

In summary, we have developed a novel Cu-catalyzed cascade cyclization reaction of enynones with a tethered alkene for the straightforward synthesis of 1*H*-indenes. The reaction was proposed to go through a copper-catalyzed 5-*exo*-*dig* cyclization of enynones to afford the key intermediate, copper (2-furyl) carbene, which then undergoes formal C(sp^2)−H insertion to provide the furyl-substituted 1*H*-indenes. In addition, the DFT calculations indicate that the proposed formal C(sp^2)−H insertion is a stepwise process, involving diene-carbene cyclization (one step but involving 6π cyclization of Cu-carbene and reductive elimination), followed by 1,5-hydrogen shift. The use of inexpensive and low toxic catalysts, mild and neutral reaction conditions, good functional-group tolerance, and high atom economy make this protocol appealing for synthetic applications.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out in oven-dried glassware under an atmosphere of dry argon. Metal catalysts used in this reaction were purchased from commercial sources and used without further purification. Solvents were dried and degassed by the standard methods. Flash column chromatography was performed using silica gel (300−400 mesh). Analytical thin-layer chromatography was performed using glass plates precoated with 200−300 mesh silica gel impregnated with a fluorescent indicator (254 nm). ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 MHz spectrometer; chemical shifts are reported in ppm with the solvent signals as reference, and coupling constants (J) are given in Hertz. The peak information is described as br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (CI Source). Enynones **1** were prepared according to the reported method.[13e]

*3-(3-(2-Styrylphenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1a**).* *trans*/*cis* = 48/52, 590.5 mg, 63% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 7.4 Hz, 2H), 7.54 (d, J = 16.3 Hz, 1H), 7.51−7.47 (comp, 2.1H), 7.45−7.38 (comp, 3H), 7.31 (t, J = 7.3 Hz, 1H), 7.28−7.13 (comp, 11.3H), 7.00 (s, 1H), 6.94 (s, 1.1H), 6.78−6.70 (comp, 2.2H), 2.54 (s, 3.2H), 2.52 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3.2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.0, 195.8, 195.7, 149.29, 149.28, 140.7, 140.1, 137.0, 136.7, 133.6, 133.1, 132.5, 131.9, 130.6, 129.9, 129.5, 129.1, 128.9, 128.40, 128.36, 128.1, 127.6, 127.5, 127.4, 127.2, 125.8, 125.0, 122.5, 122.4, 121.2, 120.6, 106.1, 105.9, 90.0, 89.4, 31.3, 31.1, 27.5, 27.4; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{19}O_2$ $[M + H]^+$: 315.1385, found 315.1379.

*3-(3-(2-(4-Methylstyryl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1b**).* *trans*/*cis* = 75/25; 608.3 mg, 62% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 1H), 7.49 (comp, 4.4H), 7.38 (t, J = 7.7 Hz, 1H), 7.23 (comp, 4.2H), 7.14 (d, J = 16.3 Hz, 1H), 7.07−7.03 (m, 0.7H), 6.97 (comp, 2H), 6.69 (s, 0.7H), 2.53 (s, 1H), 2.52 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H), 2.35 (s, 1H), 2.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.0, 195.8, 195.7, 149.21, 149.17, 140.9, 140.2, 138.4, 137.4, 134.1, 133.7, 133.6, 133.0, 132.3, 131.8, 130.5, 129.9, 129.5, 129.4, 129.0, 128.9, 127.23, 127.20, 127.18, 127.1, 124.8, 124.7, 122.5, 122.3, 121.1, 120.4, 106.1, 106.0, 89.9, 89.4, 31.2, 31.1, 27.4, 27.3, 21.4, 21.3; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_2$ $[M + H]^+$: 329.1542, found 329.1544.

*3-(3-(2-(4-Fluorostyryl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1c**).* *trans*/*cis* = 78/22; 320.1 mg, 32% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 1H), 7.65−7.58 (m, 2H), 7.52−7.43 (comp, 2.5H), 7.40 (t, J = 7.7 Hz, 1H), 7.37−7.32 (comp, 0.3H), 7.28−7.19 (comp, 2.2H), 7.16−7.01 (comp, 3.9H), 6.97 (s, 1H), 6.94−6.84 (comp, 0.8H), 6.73 (d, J = 12.2 Hz, 0.3H), 6.67 (d, J = 13.5 Hz, 0.3H), 2.53 (s, 0.8H), 2.49 (s, 3H), 2.39 (s, 3H), 2.36 (s, 0.8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.0, 195.8, 195.7, 162.8 (d, J = 248.2 Hz), 149.4, 140.4, 139.9, 133.6, 133.2, 133.1, 131.2, 130.7 (d, J = 8.0 Hz), 130.6, 130.0, 129.3, 128.9 (d, J = 8.1 Hz), 128.0 (d, J = 1.2 Hz), 127.5, 125.5 (d, J = 2.4 Hz), 124.8, 122.5, 122.2, 121.2, 120.5, 115.8 (d, J = 21.7 Hz), 115.3 (d, J = 21.4 Hz), 105.8, 105.7, 89.9, 89.4, 31.2, 31.1, 27.4, 27.2; ^{19}F NMR (376

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MHz, $CDCl_3$) δ −113.13, −113.73; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}FO_2$ $[M + H]^+$: 333.1291, found 333.1289.

*3-(3-(2-(4-Chlorostyryl)phenyl)prop-2-yn-1-ylidene)pent-ane-2,4-dione (**1d**).* *trans*/*cis* = 90:10; 586.0 mg, 56% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 1H), 7.58 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 16.5 Hz, 1H), 7.50−7.47 (m, 1H), 7.43−7.38 (m, 1H), 7.38−7.34 (m, 2H), 7.28−7.24 (m, 1H), 7.11 (d, J = 16.4 Hz, 1H), 6.96 (s, 1H), 2.49 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 195.8, 149.4, 139.7, 135.5, 134.0, 133.7, 130.6, 130.5, 129.0, 128.4, 127.7, 126.4, 124.9, 122.4, 120.7, 105.6, 90.0, 31.1, 27.2; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}ClO_2$ $[M + H]^+$: 349.0995, found 349.0991.

*3-(3-(2-(4-Bromostyryl)phenyl)prop-2-yn-1-ylidene)pent-ane-2,4-dione (**1e**).* *trans*/*cis* = 65/35; 355.4 mg, 30% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 1H), 7.58−7.45 (comp, 6.7H), 7.40 (t, J = 7.7 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.28−7.24 (comp, 1.6H), 7.24−7.18 (m, 1.7H), 7.09 (d, J = 16.3 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 6.96 (s, 1H), 6.91 (s, 0.5H), 6.78 (d, J = 12.2 Hz, 0.5H), 6.64 (d, J = 12.2 Hz, 0.5H), 2.52 (s, 1.6H), 2.49 (s, 3H), 2.39 (s, 3H), 2.36 (s, 1.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 201.0, 195.8, 195.6, 149.5, 149.4, 140.2, 139.7, 135.9, 135.5, 133.7, 133.2, 132.0, 131.5, 131.1, 130.64, 130.59, 130.5, 130.0, 129.3, 128.9, 128.7, 127.7, 127.6, 126.5, 124.9, 122.4, 122.2, 122.1, 121.5, 121.2, 120.7, 105.7, 105.6, 90.0, 89.5, 31.2, 31.1, 27.4, 27.2; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}BrO_2$ $[M + H]^+$: 393.0490, found 393.0486.

*3-(3-(2-(4-Methoxystyryl)phenyl)prop-2-yn-1-ylidene)pent-ane-2,4-dione (**1f**).* *trans*/*cis* = 75/25; 590.2 mg, 57% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 7.7 Hz, 1H), 7.57 (d, J = 8.7 Hz, 2H), 7.51−7.41 (comp, 2H), 7.41−7.35 (comp, 1.6H), 7.32−7.28 (m, 0.5H), 7.24−7.18 (comp, 1.8H), 7.16−7.07 (comp, 1.8H), 7.01−6.97 (m, 1H), 6.96−6.90 (comp, 2.4H), 6.72 (d, J = 8.8 Hz, 0.7H), 6.67−6.60 (comp, 0.7H), 3.83 (s, 3H), 3.76 (s, 1H), 2.53 (s, 1H), 2.52 (s, 3H), 2.38 (s, 3H), 2.35 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.1, 195.8, 195.7, 159.9, 159.0, 149.18, 149.15, 141.1, 140.4, 133.6, 133.1, 131.9, 131.4, 130.5, 130.4, 129.9, 129.7, 129.4, 129.1, 128.5, 127.2, 127.0, 126.3, 124.6, 123.5, 122.6, 122.4, 121.1, 120.2, 114.3, 113.7, 106.2, 106.1, 89.9, 89.3, 55.4, 55.3, 31.3, 31.1, 27.4, 27.3; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_3$ $[M + H]^+$: 345.1491, found 345.1497.

*3-(3-(2-(4-Nitrostyryl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1g**).* *trans*/*cis* = 50/50; 482.0 mg, 45% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31−8.21 (m, 2H), 8.09−8.02 (m, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.81−7.73 (comp, 2H), 7.53 (d, J = 7.6 Hz, 2H), 7.46 (t, J = 7.7 Hz, 1H), 7.36−7.27 (m, 4H), 7.26−7.19 (m, 2H), 7.16 (d, J = 7.7 Hz, 1H), 7.01−6.91 (comp, 3H), 6.79 (d, J = 12.2 Hz, 1H), 2.53 (s, 3H), 2.50 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 200.9, 195.8, 195.6, 149.8, 149.7, 147.2, 146.8, 143.5, 143.4, 139.4, 138.9, 133.8, 133.4, 131.9, 130.7, 130.3, 130.17, 130.15, 129.8, 129.2, 128.5, 128.2, 127.8, 125.2, 124.2, 123.7, 122.3, 121.8, 121.33, 121.30, 105.0, 104.9, 90.3, 89.7, 31.2, 31.1, 27.3, 27.1; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}NO_4$ $[M + H]^+$: 360.1236, found 360.1245.

*3-(3-(2-(3-Methylstyryl)phenyl)prop-2-yn-1-ylidene)pent-ane-2,4-dione (**1h**).* *trans*/*cis* = 61/39; 611.2 mg, 62% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 2H), 7.56−7.46 (comp, 7.1H), 7.44−7.38 (comp, 4.3H), 7.32−7.27 (comp, 2.6H), 7.27−7.19 (comp, 4.2H), 7.19−7.10 (comp, 4.9H), 7.10−7.05 (m, 0.8H), 7.01−6.93 (comp, 4.6H), 6.74 (d, J = 12.3 Hz, 0.7H), 6.70 (d, J = 12.3 Hz, 0.7H), 2.54 (s, 1.9H), 2.52 (s, 3H), 2.42 (s, 6.3H), 2.39 (s, 6.2H), 2.36 (s, 1.9H), 2.24 (s, 1.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.0, 195.8, 195.7, 149.2, 140.8, 140.2, 138.5, 137.9, 136.9, 136.6, 133.7, 133.1, 132.6, 132.0, 130.6, 129.9, 129.8, 129.5, 129.3, 128.7, 128.3, 128.2, 127.82, 127.76, 127.4, 127.3, 126.0, 125.5, 124.9, 124.5, 122.5, 122.4, 121.2, 120.5, 106.1, 105.9, 89.9, 89.4, 31.3, 31.1, 27.4, 27.3, 21.5, 21.4; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_2$ $[M + H]^+$: 329.1542, found 329.1548.

*3-(3-(2-(2-Methylstyryl)phenyl)prop-2-yn-1-ylidene)pent-ane-2,4-dione (**1i**).* *trans*/*cis* = 58/42; 551.2 mg, 56% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.2 Hz, 2H), 7.52−7.48 (m, 1H), 7.47−7.39 (comp, 3.8H), 7.31−7.11 (comp, 6.9H), 7.07 (m, 0.7H), 7.04−6.96 (comp, 3.8H), 6.90 (d, J = 12.2 Hz, 0.7H), 6.83 (d, J = 12.2 Hz, 0.7H), 2.57 (s, 2.1H), 2.50 (s, 3H), 2.44 (s, 3H), 2.38 (s, 2.1H), 2.38 (s, 3H), 2.28 (s, 2.1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 200.9, 195.8, 195.7, 149.4, 149.3, 140.3, 140.2, 136.3, 136.1, 135.9, 133.5, 133.0, 131.8, 130.5, 130.2, 129.7, 129.5, 129.2, 129.1, 128.28, 128.25, 127.6, 127.4, 127.1, 127.0, 126.5, 126.0, 125.7, 125.1, 122.4, 122.3, 121.2, 120.6, 106.0, 105.8, 89.9, 89.6, 31.2, 31.1, 27.4, 27.3, 20.00, 19.97; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_2$ $[M + H]^+$: 329.1542, found 329.1543.

*3-(3-(2-(2-Bromostyryl)phenyl)prop-2-yn-1-ylidene)pent-ane-2,4-dione (**1j**).* *trans*/*cis* = 8/92; 525.2 mg, 45% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.54 (m, 1H), 7.47−7.42 (m, 1H), 7.18 (t, J = 7.4 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 7.09−6.98 (m, 4H), 6.97 (s, 1H), 6.90 (d, J = 12.1 Hz, 1H), 6.80 (d, J = 12.1 Hz, 1H), 2.54 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 195.7, 149.4, 139.5, 137.3, 133.1, 132.8, 131.8, 130.9, 129.8, 129.4, 129.3, 129.0, 127.4, 127.1, 124.0, 122.3, 121.3, 105.7, 89.5, 31.2, 27.4; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}BrO_2$ $[M + H]^+$: 393.0490, found 393.0501.

*3-(3-(2-(2-(Benzo[d][1,3]dioxol-5-yl)vinyl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1k**).* *trans*/*cis* = 84/16; 336.0 mg, 31% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.0 Hz, 1H), 7.49−7.42 (comp, 1.3H), 7.41−7.32 (comp, 2.1H), 7.30−7.24 (comp, 1.4H), 7.24−7.15 (comp, 1.5H), 7.07 (d, J = 16.2 Hz, 1H), 7.02−6.90 (comp, 2.3H), 6.80 (d, J = 8.0 Hz, 1H), 6.68−6.57 (comp, 0.9H), 5.97 (s, 2H), 5.88 (s, 0.4H), 2.51 (s, 3.6H), 2.37 (s, 3H), 2.34 (s, 0.6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 200.9, 195.8, 195.7, 149.22, 149.15, 148.3, 147.9, 147.5, 147.0, 140.7, 140.1, 133.6, 133.1, 131.9, 131.5, 131.4, 130.6, 130.5, 130.0, 129.4, 127.3, 127.1, 126.8, 124.6, 123.9, 123.4, 122.6, 122.5, 122.3, 121.1, 120.3, 108.8, 108.5, 108.3, 106.1, 105.9, 101.3, 101.1, 90.0, 89.3, 31.2, 31.1, 27.4, 27.2; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{19}O_4$ $[M + H]^+$: 359.1283, found 359.1289.

*3-(3-(2-(2-(Naphthalen-1-yl)vinyl)phenyl)prop-2-yn-1-ylidene)-pentane-2,4-dione (**1l**).* *trans*/*cis* = 77/23; 439.8 mg, 40% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J = 7.9 Hz, 1H), 8.12−8.07 (m, 0.3H), 7.99 (d, J = 16.0 Hz, 1H), 7.93−7.83 (comp, 4.5H), 7.75 (d, J = 8.0 Hz, 0.3H), 7.61−7.40 (comp, 7.5H), 7.33−7.24 (comp, 2.3H), 7.21 (d, J = 7.1 Hz, 0.3H), 7.14−7.07 (comp, 0.6H), 7.02−6.94 (comp, 1.7H), 6.78 (s, 0.3H), 2.54 (s, 0.9H), 2.46 (s, 3H), 2.36 (s, 3H), 2.35 (s, 0.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.0, 195.8, 195.7, 149.34, 149.25, 140.2, 140.0, 134.5, 134.4, 133.82, 133.76, 133.6, 133.0, 131.6, 131.5, 131.0, 130.6, 129.8, 129.7, 129.4, 128.84, 128.77, 128.74, 128.65, 127.9, 127.6, 127.2, 126.9, 126.4, 126.3, 126.1, 126.0, 125.9, 125.6, 125.3, 124.7, 124.4, 123.6, 122.3, 121.2, 120.7, 106.1, 105.8, 89.9, 89.5, 31.2, 31.1, 27.4, 27.3; HRMS (TOF MS CI$^+$) calculated for $C_{26}H_{21}O_2$ $[M + H]^+$: 365.1542, found 365.1541.

*3-(3-(2-(2-(Thiophen-2-yl)vinyl)phenyl)prop-2-yn-1-ylidene) pentane-2,4-dione (**1m**).* *trans*/*cis* = 88/12; 330.8 mg, 34% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 1H), 7.61−7.57 (m, 0.15H), 7.55−7.50 (m, 1.15H), 7.46−7.38 (m, 1.37H), 7.36 (s, 2H), 7.33−7.23 (m, 3.5H), 7.13 (d, J = 5.0 Hz, 0.15H), 7.11−7.07 (m, 1H), 7.06 (s, 1H), 7.00 (d, J = 3.5 Hz, 0.14H), 6.96−6.91 (m, 0.29H), 6.87 (d, J = 12.0 Hz, 0.14H), 6.64 (d, J = 12.0 Hz, 0.13H), 2.62 (s, 3H), 2.52 (s, 0.4H), 2.44 (s, 3H), 2.38 (s, 0.4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 195.8, 149.1, 142.4, 139.5, 133.7, 130.5, 127.9, 127.4, 127.2, 125.6, 125.2, 124.8, 124.6, 122.5, 120.3, 105.8, 90.1, 31.2, 27.5; HRMS (TOF MS CI$^+$) calculated for $C_{20}H_{17}O_2S$ $[M + H]^+$: 321.0949, found 321.0957.

*3-(3-(2-(4-Phenylbuta-1,3-dien-1-yl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1n**).* *trans*/*cis* = 77/23; 422.7 mg, 41% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 1H), 7.59−7.47 (comp, 4H), 7.45−7.37 (comp, 4H), 7.37−7.21 (comp, 4H), 7.20−7.13 (comp, 2H), 7.11−6.97 (comp, 3H), 6.85−6.72 (comp, 1.7H), 6.65−6.56 (comp, 0.6H), 2.61 (s, 3H), 2.60 (s, 0.9H), 2.44 (s, 3H), 2.40 (s, 0.9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.24, 201.16, 195.8, 195.7, 149.5, 149.4, 140.4, 140.1, 137.2, 137.1, 136.0, 134.5, 133.3, 133.2, 132.2, 132.1, 130.5, 130.1, 129.8, 129.3,

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128.81, 128.75, 128.10, 128.07, 128.0, 127.3, 126.8, 126.7, 124.8, 124.7, 122.3, 122.2, 121.2, 120.2, 105.9, 105.8, 90.0, 89.7, 31.23, 31.21, 27.3, 27.2; HRMS (TOF MS CI$^+$) calculated for $C_{24}H_{21}O_2$ [M + H]$^+$: 341.1542, found 341.1536.

*(E)-3-(3-(2-(4-Phenylbut-1-en-3-yn-1-yl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1o**).* 246.6 mg, 24% yield. Yellow solid; mp 83−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.9 Hz, 1H), 7.54−7.50 (m, 2H), 7.47 (d, J = 7.4 Hz, 1H), 7.45−7.32 (m, 5H), 7.31−7.25 (m, 1H), 6.99 (s, 1H), 6.47 (d, J = 16.2 Hz, 1H), 2.60 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 195.7, 149.7, 138.7, 138.3, 133.5, 131.8, 130.5, 128.6, 128.54, 128.45, 124.7, 123.3, 122.0, 120.5, 111.2, 104.9, 93.5, 90.1, 88.9, 31.2, 27.4; HRMS (TOF MS CI$^+$) calculated for $C_{24}H_{19}O_2$ [M + H]$^+$: 339.1385, found 339.1389.

*3-(3-(2-(2-Cyclopropylvinyl)phenyl)prop-2-yn-1-ylidene)-pentane-2,4-dione (**1p**).* *trans*/*cis* = 93/7; 530.3 mg, 64% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.30 (t, J = 7.7 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 6.97 (s, 1H), 6.87 (d, J = 15.7 Hz, 1H), 5.78 (dd, J = 15.7, 9.2 Hz, 1H), 2.56 (s, 3H), 2.37 (s, 3H), 1.74−1.65 (m, 1H), 0.92−0.85 (m, 2H), 0.58−0.52 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 195.7, 149.2, 140.5, 138.8, 133.2, 130.4, 126.5, 124.8, 124.5, 122.5, 119.2, 106.3, 89.5, 31.2, 27.3, 15.1, 7.8; HRMS (TOF MS CI$^+$) calculated for $C_{19}H_{19}O_2$ [M + H]$^+$: 279.1385, found 279.1388.

*3-(3-(2-(2-Cyclohexylvinyl)phenyl)prop-2-yn-1-ylidene)-pentane-2,4-dione (**1q**).* *trans*/*cis* = 89/11; 390.4 mg, 41% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 6.98 (s, 1H), 6.73 (d, J = 15.9 Hz, 1H), 6.24 (dd, J = 15.9, 7.2 Hz, 1H), 2.55 (s, 3H), 2.36 (s, 3H), 2.28−2.15 (m, 1H), 1.87−1.73 (m, 4H), 1.72−1.64 (m, 1H), 1.39−1.27 (m, 2H), 1.27−1.07 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 195.7, 149.0, 140.7, 140.3, 133.2, 130.4, 126.7, 124.9, 124.8, 122.5, 119.7, 106.3, 89.4, 41.6, 32.9, 31.2, 27.4, 26.2, 26.0; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{25}O_2$ [M + H]$^+$: 321.1855, found 321.1859.

*3-(3-(2-Vinylphenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1r**).* 328.0 mg, 46% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 7.7 Hz, 1H), 7.41−7.34 (m, 1H), 7.27−7.21 (m, 1H), 7.10 (dd, J = 17.5, 11.0 Hz, 1H), 6.98−6.91 (m, 1H), 5.88−5.76 (m, 1H), 5.45−5.34 (m, 1H), 2.53 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 195.7, 149.4, 140.1, 134.3, 133.2, 130.5, 127.8, 125.0, 122.2, 120.3, 117.0, 105.5, 89.5, 31.2, 27.3; HRMS (TOF MS CI$^+$) calculated for $C_{16}H_{15}O_2$ [M + H]$^+$: 239.1072, found 239.1068.

*Ethyl (E)-3-(2-(4-acetyl-5-oxohex-3-en-1-yn-1-yl)phenyl)acrylate (**1s**).* 538.8 mg, 58% yield. Yellow solid; mp 66−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 16.0 Hz, 1H), 7.65 (d, J = 7.8 Hz, 1H), 7.56−7.47 (m, 1H), 7.45−7.33 (m, 2H), 6.97 (s, 1H), 6.50 (d, J = 16.0 Hz, 1H), 4.29 (q, J = 7.1 Hz, 2H), 2.57 (s, 3H), 2.38 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 195.7, 166.6, 149.9, 141.4, 136.7, 133.8, 130.5, 130.0, 126.4, 122.3, 121.8, 121.1, 104.0, 90.4, 60.9, 31.1, 27.4, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{19}H_{19}O_4$ [M + H]$^+$: 311.1283, found 311.1280.

*Ethyl (E)-3-(2-(4-benzoyl-5-oxo-5-phenylpent-3-en-1-yn-1-yl)-phenyl)acrylate (**1t**).* 764.3 mg, 59% yield. Yellow solid; mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−7.99 (m, 2H), 7.93 (d, J = 16.0 Hz, 1H), 7.86−7.80 (m, 2H), 7.59−7.52 (comp, 3H), 7.49−7.42 (comp, 4H), 7.30 (t, J = 7.6 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.02 (s, 1H), 6.95 (d, J = 7.5 Hz, 1H), 6.43 (d, J = 16.0 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 193.0, 166.6, 148.5, 141.5, 136.7, 136.36, 136.35, 133.9, 133.7, 133.2, 130.1, 129.7, 129.6, 129.4, 128.9, 128.8, 126.2, 123.9, 122.3, 120.8, 103.4, 90.6, 60.8, 14.4; HRMS (TOF MS CI$^+$) calculated for $C_{29}H_{23}O_4$ [M + H]$^+$: 435.1596, found 435.1602.

*Ethyl 3-(2-(4-(4-chlorobenzoyl)-5-(4-chlorophenyl)-5-oxopent-3-en-1-yn-1-yl)phe nyl)acrylate (**1u**).* *trans*/*cis* = 98/2; 772.1 mg, 51% yield. Yellow solid; mp 126−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.5 Hz, 2H), 7.89 (d, J = 16.0 Hz, 1H), 7.81−7.72 (m, 2H), 7.57 (d, J = 7.9 Hz, 1H), 7.47−7.40 (comp, 4H), 7.33 (t, J = 7.7 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.06−6.93 (m, 2H), 6.44 (d, J = 16.0 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 191.5, 166.6, 147.6, 141.3, 140.6, 139.9, 136.5, 134.9, 134.6, 133.6, 131.1, 130.8, 130.3, 129.7, 129.3, 129.2, 126.2, 124.2, 122.0, 120.9, 104.0, 90.2, 60.8, 14.4; HRMS (TOF MS CI$^+$) calculated for $C_{29}H_{21}Cl_2O_4$ [M + H]$^+$: 503.0817, found 503.0833.

*Methyl 2-acetyl-5-(2-((E)-3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)-pent-2-en-4-yno ate (**1v**).* *Z*/*E* = 50/50; 533.6 mg, 55% yield. Yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 16.0 Hz, 1H), 8.05 (d, J = 16.0 Hz, 1H), 7.64 (t, J = 7.3 Hz, 2H), 7.54−7.48 (m, 2H), 7.44−7.32 (comp, 4H), 7.10 (s, 1H), 7.09 (s, 1H), 6.51 (d, J = 16.0 Hz, 1H), 6.49 (d, J = 16.0 Hz, 1H), 4.32−4.23 (m, 4H), 3.93 (s, 3H), 3.83 (s, 3H), 2.53 (s, 3H), 2.42 (s, 3H), 1.37−1.29 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1, 193.9, 166.4, 165.5, 164.2, 142.2, 141.3, 141.1, 136.51, 136.45, 133.8, 133.7, 130.3, 130.2, 129.8, 129.7, 126.2, 124.6, 123.0, 122.4, 122.2, 120.9, 103.6, 102.4, 90.7, 90.3, 60.6, 52.6, 52.5, 30.4, 27.8, 14.3; HRMS (TOF MS CI$^+$) calculated for $C_{19}H_{19}O_5$ [M + H]$^+$: 327.1232, found 327.1240.

*(E)-3-(3-(2-(3-Oxo-3-phenylprop-1-en-1-yl)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1w**).* 520.8 mg, 51% yield. Yellow solid; mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 15.7 Hz, 1H), 8.04−7.98 (m, 2H), 7.79 (d, J = 7.8 Hz, 1H), 7.61−7.55 (comp, 2H), 7.54−7.47 (comp, 3H), 7.46−7.41 (m, 1H), 7.40−7.35 (m, 1H), 6.95 (s, 1H), 2.54 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 195.7, 190.1, 150.0, 141.4, 138.0, 137.0, 133.8, 133.1, 130.4, 130.1, 128.8, 128.6, 126.5, 124.5, 122.8, 121.6, 104.0, 90.6, 31.1, 27.3; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{19}O_3$ [M + H]$^+$: 343.1334, found 343.1331.

*3-(2-(4-Acetyl-5-oxohex-3-en-1-yn-1-yl)phenyl)acrylonitrile (**1x**).* *trans*/*cis* = 99/1; 197.0 mg, 25% yield. Yellow solid; mp 91−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86−7.76 (m, 1H), 7.60−7.48 (comp, 2H), 7.47−7.35 (comp, 2H), 6.90 (s, 1H), 5.99 (d, J = 16.7 Hz, 1H), 2.51 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 195.7, 150.6, 147.7, 135.5, 133.8, 130.9, 130.6, 125.7, 121.9, 121.3, 117.9, 102.6, 99.1, 90.8, 31.0, 27.1; HRMS (TOF MS CI$^+$) calculated for $C_{17}H_{14}NO_2$ [M + H]$^+$: 264.1025, found 264.1024.

*Ethyl (E)-3-(2-(4-acetyl-5-oxohex-3-en-1-yn-1-yl)phenyl)-but-2-enoate (**1y**).* 311.2 mg, 32% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.6 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.31 (t, J = 7.6 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 6.90 (s, 1H), 5.89 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.51 (s, 3H), 2.49 (s, 3H), 2.35 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 195.7, 166.4, 155.6, 149.6, 146.9, 133.7, 130.3, 128.1, 127.7, 122.0, 120.8, 119.2, 105.4, 88.7, 60.2, 31.1, 27.5, 20.4, 14.4; HRMS (TOF MS CI$^+$) calculated for $C_{20}H_{21}O_4$ [M + H]$^+$: 325.1440, found 325.1441.

*3-(3-(2-(2-(4-Methoxyphenyl)vinyl-2-d)phenyl)prop-2-yn-1-ylidene)pentane-2,4-dione (**1f−d**).* *trans*/*cis* = 58/42; 482.2 mg, 47% yield. Yellow soild; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 1H), 7.61−7.55 (m, 2H), 7.50−7.44 (m, 1.7H), 7.42−7.34 (m, 2.1H), 7.33−7.28 (m, 0.8H), 7.24−7.16 (m, 2.6H), 7.13−7.07 (m, 1.5H), 6.99 (s, 1H), 6.96−6.90 (m, 2.8H), 6.75−6.69 (m, 1.5H), 6.63 (s, 0.7H), 3.83 (s, 3H), 3.76 (s, 2.1H), 2.53 (s, 2.1H), 2.52 (s, 3H), 2.38 (s, 3H), 2.35 (s, 2.1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 201.1, 195.8, 195.7, 159.9, 159.0 149.19, 149.16 141.1, 140.4, 133.6, 133.1, 130.5, 130.3, 129.9, 129.7, 129.4, 129.0, 128.5, 127.2, 126.2, 124.7, 123.4, 122.5, 122.4, 121.1, 120.2, 114.3, 113.7, 106.2, 106.1, 89.9, 89.3, 55.4, 55.3, 31.2, 31.14, 27.4, 27.3; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{20}DO_3$ [M + H]$^+$: 346.1553, found 346.1548.

General Procedure for Copper-Catalyzed Cyclization Reaction of 1. To a 10 mL oven-dried vial containing a magnetic stirring bar, enynones **1** (0.2 mmol), $CuSO_4{\cdot}5H_2O$ (0.5 mg, 1.0 mol %) and anhydrous DCE (2.0 mL) were added in sequence under atmosphere of argon, and the reaction mixture was stirred at 55 °C. When the reaction was completed (monitored by TLC, 2−16 h), the solvent was evaporated in vacuo, and the residue was purified by flash column chromatography on silica gel without additional treatment (hexanes/ethyl acetate = 10:1 to 5:1) to afford the pure products **2**.

*1-(2-Methyl-5-(2-phenyl-1H-inden-3-yl)furan-3-yl)ethan-1-one (**2a**).* 59.4 mg, 95% yield. Yellow solid; mp 74−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 7.3 Hz, 1H),

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7.42−7.26 (comp, 7H), 6.64 (s, 1H), 3.90 (s, 2H), 2.60 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 157.8, 147.5, 144.5, 144.2, 142.4, 136.8, 128.4, 128.3, 127.9, 127.9, 126.9, 125.5, 123.8, 122.8, 120.9, 109.6, 42.6, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{19}O_2$ [M + H]$^+$: 315.1385, found 315.1383.

1-(2-Methyl-5-(2-(p-tolyl)-1H-inden-3-yl)furan-3-yl)ethan-1-one (**2b**). 62.2 mg, 95% yield. Yellow solid; mp 110−112 °C; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.63 (d, J = 7.6 Hz, 1H), 7.52 (d, J = 7.3 Hz, 1H), 7.35 (t, J = 7.3 Hz, 1H), 7.30 (d, J = 8.2 Hz, 2H), 7.26 (td, J = 7.4, 1.1 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 6.70 (s, 1H), 3.88 (s, 2H), 2.59 (s, 3H), 2.40 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 194.3, 157.9, 147.9, 145.1, 144.9, 142.8, 138.4, 134.2, 129.5, 128.6, 127.6, 127.1, 125.7, 124.2, 123.3, 121.0, 110.1, 42.8, 29.6, 21.6, 14.7; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_2$ [M + H]$^+$: 329.1542, found 329.1537.

1-(5-(2-(4-Fluorophenyl)-1H-inden-3-yl)-2-methylfuran-3-yl)-ethan-1-one (**2c**). 63.7 mg, 96% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.4 Hz, 1H), 7.41−7.32 (comp, 3H), 7.31−7.27 (m, 1H), 7.09−7.00 (m, 2H), 6.66 (s, 1H), 3.86 (s, 2H), 2.60 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 162.4 (d, J = 247.9 Hz), 157.9, 147.3, 144.0, 143.2, 142.2, 132.9 (d, J = 3.5 Hz), 130.0 (d, J = 8.0 Hz), 127.9, 126.9, 125.6, 123.8, 122.9, 120.9, 115.4 (d, J = 21.5 Hz), 109.7, 42.6, 29.3, 14.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −113.70; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}FO_2$ [M + H]$^+$: 333.1291, found 333.1286.

1-(5-(2-(4-Chlorophenyl)-1H-inden-3-yl)-2-methylfuran-3-yl)-ethan-1-one (**2d**). 67.4 mg, 97% yield. Yellow solid; mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.37 (t, J = 7.4 Hz, 1H), 7.33−7.31 (comp, 4H), 7.31−7.26 (m, 1H), 6.69 (s, 1H), 3.86 (s, 2H), 2.60 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 158.0, 147.1, 144.0, 142.8, 142.2, 135.2, 133.7, 129.6, 128.6, 128.4, 127.0, 125.8, 123.9, 122.9, 121.0, 109.9, 42.4, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}ClO_2$ [M + H]$^+$: 349.0995, found 349.0997.

1-(5-(2-(4-Bromophenyl)-1H-inden-3-yl)-2-methylfuran-3-yl)-ethan-1-one (**2e**). 74.5 mg, 95% yield. Yellow solid; mp 105−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.49−7.43 (m, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.32−7.27 (m, 1H), 7.26−7.22 (m, 2H), 6.70 (s, 1H), 3.84 (s, 2H), 2.60 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 158.0, 147.0, 143.9, 142.8, 142.2, 135.7, 131.6, 129.9, 128.4, 126.9, 125.8, 123.9, 122.9, 121.8, 120.9, 109.9, 42.3, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}BrO_2$ [M + H]$^+$: 393.0490, found 393.0497.

1-(5-(2-(4-Methoxyphenyl)-1H-inden-3-yl)-2-methylfuran-3-yl)-ethan-1-one (**2f**). 64.4 mg, 94% yield. Yellow solid; mp 112−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 1H), 7.49 (d, J = 7.3 Hz, 1H), 7.38−7.31 (comp, 3H), 7.28−7.23 (m, 1H), 6.92−6.86 (m, 2H), 6.67 (s, 1H), 3.86 (s, 2H), 3.84 (s, 3H), 2.62 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 159.4, 157.7, 147.6, 144.5, 144.4, 142.1, 129.6, 129.1, 126.8, 126.7, 125.2, 123.7, 122.8, 120.6, 113.9, 109.5, 55.4, 42.4, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_3$ [M + H]$^+$: 345.1491, found 345.1486.

1-(2-Methyl-5-(2-(4-nitrophenyl)-1H-inden-3-yl)furan-3-yl)-ethan-1-one (**2g**). 66.3 mg, 92% yield. Yellow solid; mp 168−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24−8.13 (m, 2H), 7.67 (d, J = 7.6 Hz, 1H), 7.55 (d, J = 7.4 Hz, 1H), 7.53−7.49 (m, 2H), 7.45−7.38 (m, 1H), 7.36−7.31 (m, 1H), 6.80 (s, 1H), 3.92 (s, 2H), 2.58 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 158.5, 146.8, 146.4, 143.5, 143.4, 142.5, 141.0, 130.9, 129.0, 127.2, 126.6, 124.1, 123.7, 123.1, 121.4, 110.6, 42.2, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}NO_4$ [M + H]$^+$: 360.1236, found 360.1243.

1-(2-Methyl-5-(2-(m-tolyl)-1H-inden-3-yl)furan-3-yl)ethan-1-one (**2h**). 62.8 mg, 96% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.31−7.26 (m, 1H), 7.26−7.21 (m, 2H), 7.18 (d, J = 7.7 Hz, 1H), 7.13 (d, J = 7.5 Hz, 1H), 6.66 (s, 1H), 3.89 (s, 2H), 2.61 (s, 3H), 2.40 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 157.7, 147.6, 144.6, 144.2, 142.4, 138.0, 136.7, 129.0, 128.6, 128.3, 127.7, 126.8, 125.48, 125.45, 123.8, 122.8, 120.9, 109.6, 42.6, 29.3, 21.6, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_2$ [M + H]$^+$: 329.1542, found 329.1540.

1-(2-Methyl-5-(2-(o-tolyl)-1H-inden-3-yl)furan-3-yl)ethan-1-one (**2i**). 59.2 mg, 90% yield. Yellow solid; mp 77−79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 7.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.34−7.25 (comp, 4H), 7.23−7.17 (m, 1H), 6.11 (s, 1H), 3.79 (s, 2H), 2.59 (s, 3H), 2.25 (s, 3H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 157.2, 148.5, 143.8, 142.9, 142.9, 137.7, 135.9, 130.3, 128.9, 128.7, 127.9, 126.8, 126.1, 125.3, 123.8, 122.6, 121.8, 108.7, 44.1, 29.1, 19.9, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{21}O_2$ [M + H]$^+$: 329.1542, found 329.1547.

1-(5-(2-(2-Bromophenyl)-1H-inden-3-yl)-2-methylfuran-3-yl)-ethan-1-one (**2j**). 73.0 mg, 93% yield. Yellow solid; mp 128−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.7 Hz, 1H), 7.71−7.66 (m, 1H), 7.54 (d, J = 7.4 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.40−7.35 (m, 1H), 7.35−7.30 (m, 1H), 7.30−7.23 (comp, 2H), 6.28 (s, 1H), 3.88 (s, 2H), 2.56 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 157.5, 147.8, 142.9, 142.6, 142.4, 139.3, 132.9, 130.5, 129.8, 129.3, 127.6, 126.8, 125.7, 123.9, 123.3, 122.7, 121.9, 109.1, 43.4, 29.1, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{18}BrO_2$ [M + H]$^+$: 393.0490, found 393.0491.

1-(5-(2-(Benzo[d][1,3]dioxol-5-yl)-1H-inden-3-yl)-2-methylfuran-3-yl)ethan-1-one (**2k**). 65.0 mg, 91% yield. Yellow solid; mp 86−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.3 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 7.28−7.22 (m, 1H), 6.93−6.88 (m, 1H), 6.85 (d, J = 1.7 Hz, 1H), 6.80 (d, J = 8.1 Hz, 1H), 6.69 (s, 1H), 5.98 (s, 2H), 3.83 (s, 2H), 2.63 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 157.8, 147.7, 147.3, 144.4, 144.1, 142.0, 130.6, 127.2, 126.8, 125.4, 123.7, 122.9, 122.2, 120.7, 109.7, 108.6, 108.4, 101.3, 42.6, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{19}O_4$ [M + H]$^+$: 359.1283, found 359.1282.

1-(2-Methyl-5-(2-(naphthalen-1-yl)-1H-inden-3-yl)furan-3-yl)-ethan-1-one (**2l**). 67.0 mg, 92% yield. Yellow solid; mp 82−84 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.7 Hz, 1H), 7.91 (t, J = 7.3 Hz, 2H), 7.75 (d, J = 8.4 Hz, 1H), 7.57 (comp, 2H), 7.47 (comp, 3H), 7.37 (comp, 2H), 6.04 (s, 1H), 3.97 (s, 2H), 2.45 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (10 MHz, $CDCl_3$) δ 194.2, 157.2, 148.0, 143.1, 142.9, 142.2, 136.1, 133.7, 131.4, 130.1, 128.4, 128.1, 126.9, 126.3, 126.2, 126.1, 125.7, 125.6, 125.5, 123.8, 122.4, 121.9, 109.3, 45.2, 28.9, 14.3; HRMS (TOF MS CI$^+$) calculated for $C_{26}H_{21}O_2$ [M + H]$^+$: 365.1542, found 365.1547.

1-(2-Methyl-5-(2-(thiophen-2-yl)-1H-inden-3-yl)furan-3-yl)-ethan-1-one (**2m**). 62.0 mg, 97% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 7.3 Hz, 1H), 7.44 (d, J = 7.5 Hz, 1H), 7.34 (t, J = 7.4 Hz, 1H), 7.32−7.29 (m, 1H), 7.29−7.24 (comp, 2H), 7.05 (dd, J = 5.1, 3.7 Hz, 1H), 6.91 (s, 1H), 3.99 (s, 2H), 2.73 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 158.5, 145.9, 144.9, 141.2, 138.7, 138.6, 127.3, 127.0, 126.9, 126.8, 126.5, 125.7, 123.7, 123.0, 120.5, 111.0, 42.1, 29.4, 14.7; HRMS (TOF MS CI$^+$) calculated for $C_{20}H_{17}O_2S$ [M + H]$^+$: 321.0949, found 321.0947.

(E)-1-(2-Methyl-5-(2-styryl-1H-inden-3-yl)furan-3-yl)ethan-1-one (**2n**). 60.1 mg, 88% yield. Yellow solid; mp 139−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.64 (m, 2H), 7.49 (comp, 3H), 7.32 (comp, 5H), 6.94 (d, J = 14.4 Hz, 2H), 3.85 (s, 2H), 2.76 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 158.3, 148.0, 143.4, 142.1, 142.0, 137.5, 131.7, 129.4, 128.9, 128.0, 126.9, 126.7, 125.9, 123.9, 123.6, 123.1, 121.0, 110.2, 38.3, 29.4, 14.9; HRMS (TOF MS CI$^+$) calculated for $C_{24}H_{21}O_2$ [M + H]$^+$: 341.1542, found 341.1543.

1-(2-Methyl-5-(2-(phenylethynyl)-1H-inden-3-yl)furan-3-yl)-ethan-1-one (**2o**). 63.5 mg, 94% yield. Yellow solid; mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.7 Hz, 1H), 7.59−7.53 (comp, 3H), 7.47 (d, J = 7.3 Hz, 1H), 7.42−7.36 (comp, 4H), 7.35−7.30 (m, 1H), 3.77 (s, 2H), 2.75 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 157.7, 148.6, 142.7, 141.5, 136.0, 131.5, 128.7, 128.7, 127.1, 126.5, 123.8, 123.5, 122.9, 122.7, 120.4, 110.8, 100.2, 87.9, 42.8, 29.3, 14.8; HRMS (TOF MS CI$^+$) calculated for $C_{24}H_{19}O_2$ [M + H]$^+$: 339.1385, found 339.1382.

1-(5-(2-Cyclopropyl-1H-inden-3-yl)-2-methylfuran-3-yl)ethan-1-one (**2p**). 52.7 mg, 95% yield. Yellow solid; mp 81−82 °C; ^{1}H NMR

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(400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.7 Hz, 1H), 7.38 (d, J = 7.4 Hz, 1H), 7.31 (t, J = 7.5 Hz, 1H), 7.17 (td, J = 7.4, 1.0 Hz, 1H), 6.85 (s, 1H), 3.20 (s, 2H), 2.71 (s, 3H), 2.49 (s, 3H), 2.40−2.30 (m, 1H), 1.09−0.98 (m, 2H), 0.82−0.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 157.2, 148.9, 148.4, 143.9, 140.9, 127.5, 126.6, 124.4, 123.6, 122.8, 119.8, 108.6, 37.6, 29.4, 14.7, 12.4, 9.2; HRMS (TOF MS CI$^+$) calculated for $C_{19}H_{19}O_2$ $[M + H]^+$: 279.1385, found 279.1379.

1-(5-(2-Cyclohexyl-1H-inden-3-yl)-2-methylfuran-3-yl)ethan-1-one (**2q**). 62.5 mg, 98% yield. Yellow solid; mp 81−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 7.3 Hz, 1H), 7.33 (t, J = 7.3 Hz, 1H), 7.21 (td, J = 7.4, 1.0 Hz, 1H), 6.73 (s, 1H), 3.50 (s, 2H), 3.15−2.80 (m, 1H), 2.71 (s, 3H), 2.50 (s, 3H), 1.93−1.75 (comp, 5H), 1.50−1.24 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.2, 157.3, 153.5, 148.0, 143.7, 142.1, 126.5, 125.8, 124.5, 123.7, 122.8, 120.2, 108.5, 39.1, 38.1, 33.2, 29.3, 26.6, 26.2, 14.7; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{25}O_2$ $[M + H]^+$: 321.1855, found 321.1852.

1-(5-(1H-Inden-3-yl)-2-methylfuran-3-yl)ethan-1-one (**2r**). 40.0 mg, 84% yield. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 7.5 Hz, 1H), 7.53 (d, J = 7.2 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 7.29 (t, J = 7.3 Hz, 1H), 6.93 (s, 1H), 6.84 (s, 1H), 3.54 (s, 2H), 2.68 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.1, 157.8, 148.3, 144.4, 141.3, 133.4, 129.7, 126.5, 125.4, 124.2, 122.9, 120.6, 106.8, 38.3, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{16}H_{15}O_2$ $[M + H]^+$: 239.1072, found 239.1069.

Ethyl 3-(4-acetyl-5-methylfuran-2-yl)-1H-indene-2-carboxylate (**2s**). 56.4 mg, 91% yield. Yellow solid; mp 87−90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04−7.99 (m, 1H), 7.71 (s, 1H), 7.55−7.49 (m, 1H), 7.42−7.37 (m, 2H), 4.31 (q, J = 7.1 Hz, 2H), 3.89 (s, 2H), 2.73 (s, 3H), 2.51 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.6, 165.0, 158.9, 146.4, 143.5, 142.4, 139.3, 130.0, 128.0, 127.1, 124.5, 124.2, 122.9, 115.8, 60.7, 40.5, 29.4, 14.7, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{19}H_{19}O_4$ $[M + H]^+$: 311.1283, found 311.1277.

Ethyl 3-(4-benzoyl-5-phenylfuran-2-yl)-1H-indene-2-carboxylate (**2t**). 73.4 mg, 85% yield. Yellow solid; mp 123−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17−8.10 (m, 1H), 8.00−7.94 (m, 2H), 7.89−7.83 (m, 2H), 7.72 (s, 1H), 7.58−7.53 (comp, 2H), 7.48−7.41 (comp, 4H), 7.41−7.35 (comp, 3H), 4.30 (q, J = 7.1 Hz, 2H), 3.94 (s, 2H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 164.9, 155.6, 147.0, 143.4, 142.3, 138.8, 138.0, 133.2, 131.0, 130.0, 129.7, 129.5, 128.6, 128.6, 128.0, 127.7, 127.2, 124.3, 124.2, 122.5, 118.7, 60.7, 40.6, 14.4; HRMS (TOF MS CI$^+$) calculated for $C_{29}H_{23}O_4$ $[M + H]^+$: 435.1596, found 435.1587.

Ethyl 3-(4-(4-chlorobenzoyl)-5-(4-chlorophenyl)furan-2-yl)-1H-indene-2-carboxylate (**2u**). 82.0 mg, 82% yield. Yellow solid; mp 176−177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09−8.03 (m, 1H), 7.94−7.89 (m, 2H), 7.88−7.81 (m, 2H), 7.68 (s, 1H), 7.58−7.53 (m, 1H), 7.47−7.40 (comp, 4H), 7.40−7.35 (m, 2H), 4.30 (q, J = 7.1 Hz, 2H), 3.94 (s, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 164.8, 154.7, 147.3, 143.4, 142.1, 139.8, 138.7, 136.3, 135.7, 131.5, 131.4, 129.0, 129.0, 128.9, 128.2, 128.0, 127.2, 124.3, 124.1, 122.4, 118.7, 60.8, 40.6, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{29}H_{21}Cl_2O_4$ $[M + H]^+$: 503.0817, found 503.0812.

Methyl 5-(2-(ethoxycarbonyl)-1H-inden-3-yl)-2-methylfuran-3-carboxylate (**2v**). 53.0 mg, 81% yield. Yellow solid; mp 121−122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00−7.93 (m, 1H), 7.61 (s, 1H), 7.54−7.48 (m, 1H), 7.41−7.35 (comp, 2H), 4.30 (q, J = 7.1 Hz, 2H), 3.871 (s, 2H), 3.865 (s, 3H), 2.72 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 164.5, 159.6, 146.4, 143.4, 142.4, 139.0, 130.3, 127.9, 127.0, 124.3, 124.1, 115.5, 115.1, 60.6, 51.6, 40.4, 14.4, 14.1; HRMS (TOF MS CI$^+$) calculated for $C_{19}H_{19}O_5$ $[M + H]^+$: 327.1232, found 327.1226.

1-(5-(2-Benzoyl-1H-inden-3-yl)-2-methylfuran-3-yl)ethan-1-one (**2w**). 24.1 mg, 35% yield. Yellow solid; mp 117−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (m, 1H), 7.78−7.71 (m, 2H), 7.60 (d, J = 6.9 Hz, 1H), 7.49−7.40 (comp, 3H), 7.32 (t, J = 7.7 Hz, 2H), 6.87 (s, 1H), 4.02 (s, 2H), 2.34 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 193.8, 158.9, 145.6, 143.5, 141.5, 140.0, 138.5, 135.5, 132.6, 128.9, 128.3, 127.7, 127.3, 124.6, 122.8, 122.5, 111.9, 41.2, 29.2, 14.1; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{19}O_3$ $[M + H]^+$: 343.1334, found 343.1331.

3-(4-Acetyl-5-methylfuran-2-yl)-1H-indene-2-carbonitrile (**2x**). 27.5 mg, 52% yield. Yellow solid; mp 162−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17−8.03 (m, 1H), 7.58−7.50 (comp, 2H), 7.50−7.42 (comp, 2H), 3.83 (s, 2H), 2.77 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 159.9, 145.8, 144.0, 143.3, 139.2, 128.9, 127.8, 124.4, 124.0, 123.3, 118.0, 113.4, 105.1, 40.8, 29.4, 14.8; HRMS (TOF MS CI$^+$) calculated for $C_{17}H_{14}NO_2$ $[M + H]^+$: 264.1025, found 264.1026.

General Procedure for Scale Up. To a 50 mL oven-dried round-bottom flask with a magnetic stirring bar, enynone **1j** (1.18 g, 3.0 mmol), $CuSO_4{\cdot}5H_2O$ (7.5 mg, 1.0 mol %), and anhydrous DCE (15.0 mL) was added in sequence under atmosphere of argon, and the reaction mixture was stirred at 55 °C for 2 h. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo and the residue was purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 5:1) to give 1.11 g of pure **2j** (94% yield).

Procedure for the Preparation of 3j.[25] To a 10 mL oven-dried vial containing a magnetic stirring bar, **2j** (39.3 mg, 0.1 mmol), AIBN (32.8 mg, 0.2 mmol), n-Bu_3SnH (40 μL, 0.15 mmol) and anhydrous toluene (2.0 mL) were added in sequence under atmosphere of argon, and the reaction mixture was stirred at 110 °C for 30 min. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo and the residue was purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 5:1) to afford 25.0 mg of pure **3j** (80% yield). Yellow solid; mp 200−202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67−8.59 (m, 1H), 8.10 (d, J = 7.5 Hz, 1H), 8.03−7.96 (m, 1H), 7.60 (d, J = 7.4 Hz, 1H), 7.56−7.49 (m, 2H), 7.45 (t, J = 7.4 Hz, 1H), 7.39−7.32 (m, 1H), 4.12 (s, 2H), 2.78 (s, 3H), 2.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 157.5, 147.3, 143.5, 140.0, 138.8, 128.5, 127.1, 127.0, 126.5, 126.4, 125.8, 125.5, 125.1, 124.9, 124.7, 122.4, 121.9, 120.4, 36.7, 32.2, 15.4; HRMS (TOF MS CI$^+$) calculated for $C_{22}H_{17}O_2$ $[M + H]^+$: 313.1229, found 313.1224.

Procedure for the Preparation of 4j. To a 25 mL oven-dried round-bottom flask with a magnetic stirring bar, **2j** (78.4 mg, 0.2 mmol), 4-methoxyphenylboronic acid (60.8 mg, 0.4 mmol), Na_2CO_3 (53 mg, 0.5 mmol), $Pd(PPh_3)_4$ (11.6 mg, 5 mol %), water (0.5 mL) and DME (3.5 mL) were added in sequence under atmosphere of argon, and the reaction mixture was heated to reflux overnight. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo and the residue was purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 4:1) to afford 65.5 mg of pure **4j** (78% yield). Yellow solid; mp 78−80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 1H), 7.42 (comp, 2H), 7.33 (comp, 4H), 7.24−7.19 (m, 1H), 7.18−7.08 (m, 2H), 6.81−6.68 (m, 2H), 6.33 (s, 1H), 3.74 (s, 3H), 3.44 (s, 2H), 2.57 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194., 158.7, 157.4, 148.2, 144.9, 143.1, 143.0, 140.7, 136.4, 133.8, 130.3, 130.1, 129.9, 129.5, 128.2, 127.1, 126.6, 125.2, 123.7, 122.7, 121.3, 113.8, 109.1, 55.3, 43.2, 29.2, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{29}H_{25}O_3$ $[M + H]^+$: 421.1804, found 421.1802.

Procedure for the Preparation of 2y and 2y′. To a 10 mL oven-dried vial containing a magnetic stirring bar, **1y** (64.8 mg, 0.2 mmol), $CuSO_4{\cdot}5H_2O$ (0.5 mg, 1.0 mol %) and anhydrous DCE (2.0 mL) was added in sequence under atmosphere of argon, and the reaction mixture was stirred at 55 °C for 16 h. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo, and the residue was purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 7.5:1) to afford 41.0 mg of **2y** and 4.0 mg of **2y′** in total 70% yield.

To a 10 mL oven-dried vial containing a magnetic stirring bar, **1y** (64.8 mg, 0.2 mmol), CuCl (1.0 mg, 5.0 mol %) and anhydrous DCE (2.0 mL) was added in sequence under atmosphere of argon, and the reaction mixture was stirred at room temperature for 16 h. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo and the residue was purified by flash column

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chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 7.5:1) to afford 40.8 mg of **2y** and 12.3 mg of **2y′** in total 82% yield.

*Ethyl 3-(4-acetyl-5-methylfuran-2-yl)-1-methyl-1H-indene-2-carboxylate (**2y**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.89 (m, 1H), 7.55 (s, 1H), 7.51−7.45 (m, 1H), 7.43−7.35 (m, 2H), 4.42−4.24 (m, 2H), 3.98 (q, J = 7.4 Hz, 1H), 2.72 (s, 3H), 2.50 (s, 2H), 1.48 (d, J = 7.4 Hz, 3H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.4, 165.1, 158.9, 149.5, 146.2, 140.7, 137.7, 136.3, 128.2, 127.2, 124.2, 123.3, 122.9, 115.0, 60.7, 46.0, 29.4, 16.9, 14.7, 14.5; HRMS (TOF MS CI$^+$) calculated for $C_{20}H_{21}O_4$ $[M + H]^+$: 325.1440, found 325.1436.

*Ethyl 1-(4-acetyl-5-methylfuran-2-yl)-3-methyl-1H-indene-2-carboxylate (**2y′**).* Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.49 (m, 1H), 7.43−7.32 (m, 3H), 6.31 (s, 1H), 4.94 (d, J = 2.1 Hz, 1H), 4.36−4.12 (m, 2H), 2.60 (d, J = 2.2 Hz, 3H), 2.50 (s, 3H), 2.34 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 165.2, 157.6, 152.9, 150.3, 145.1, 143.9, 131.0, 128.7, 127.8, 124.1, 122.3, 121.7, 106.5, 60.2, 48.9, 29.3, 14.6, 14.4, 12.8; HRMS (TOF MS CI$^+$) calculated for $C_{20}H_{21}O_4$ $[M + H]^+$: 325.1440, found 325.1436.

Control Experiment of 2y and 2y′. To a 10 mL oven-dried vial containing a magnetic stirring bar, **2y′** (32.4 mg, 0.1 mmol), $CuSO_4 \cdot 5H_2O$ (0.3 mg, 1.0 mol %) and anhydrous DCE (1.0 mL) was added in sequence under atmosphere of argon. After stirring for 16 h at 55 °C, the reaction mixture was concentrated in vacuo. The residue was subjected to proton NMR analysis and only signals of compound **2y′** was observed.

To a 10 mL oven-dried vial containing a magnetic stirring bar, **2y** (32.4 mg, 0.1 mmol), $CuSO_4 \cdot 5H_2O$ (0.3 mg, 1.0 mol %) and anhydrous DCE (1.0 mL) was added in sequence under atmosphere of argon. After stirring for 16 h at 55 °C, the reaction mixture was concentrated in vacuo. The residue was subjected to proton NMR analysis and only signals of compound **2y** was observed.

Isotope-Labeled Experiment. To a 10 mL oven-dried vial containing a magnetic stirring bar, **1f-*d*** (>95% D, 34.5 mg, 0.1 mmol), $CuSO_4 \cdot 5H_2O$ (0.3 mg, 1.0 mol %) and anhydrous DCE (2.0 mL) was added in sequence under atmosphere of argon, and the reaction mixture was stirred at 55 °C for 2 h. When the reaction was completed (monitored by TLC), the solvent was evaporated in vacuo and the residue was purified by flash column chromatography on silica gel (hexanes/ethyl acetate = 10:1 to 7.5:1) to afford 31.8 mg of pure **2f-*d*** (92% yield, > 95% D, see Figure S1). **2f-*d***: Yellow solid; mp 113−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.37 (comp, 3H), 7.30−7.25 (m, 1H), 6.94−6.89 (m, 2H), 6.70 (s, 1H), 3.86 (s, 4H), 2.65 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.3, 159.4, 157.7, 147.6, 144.6, 144.3, 142.0, 129.5, 129.1, 126.8, 126.7, 125.2, 123.7, 122.8, 120.5, 113.8, 109.5, 55.4, 29.3, 14.6; HRMS (TOF MS CI$^+$) calculated for $C_{23}H_{20}DO_3$ $[M + H]^+$: 346.1553, found 346.1549.

Computational Methods. All of the calculations were performed with the Gaussian 09 program.[26] Geometry optimizations of all the minima and transition states involved were carried out at the B3LYP level of theory[27] in the gas phase. The SDD basis set[28] and pseudopotential were used for Cu and the 6-31G(d) basis set[29] for the other atoms. The key word "5D" was used to specify that five d-type orbitals were used for all elements in the calculations. For open-shell species, (U)B3LYP method was used. Frequency calculations at the same level were performed to validate each structure as either a minimum or a transition state and to evaluate its zero-point energy and the thermal corrections at 298 K. Key transition-state structures were confirmed to connect corresponding reactants and products by intrinsic reaction coordinate (IRC) calculations.[30] Solvation energies in dichloroethane (ε = 10.125) were evaluated by IEFPCM calculations with radii and nonelectrostatic terms for SMD solvation model[31] using the gas-phase optimized structures. Standard state concentrations of 1.0 mol/L were used for all species in calculations. To improve the calculation accuracy, single-point energies calculations were computed at the B3LYP level of theory with the SDD basis set and pseudopotential for Cu and the 6-311+G(d,p) basis set[32] for the other atoms.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.8b02064.

Computational results, ^{1}H and ^{13}C NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: yuzx@pku.edu.cn.

*E-mail: xinfangxu@suda.edu.cn.

ORCID

Zhi-Xiang Yu: 0000-0003-0939-9727

Xin-Fang Xu: 0000-0002-8706-5151

Notes

The authors declare no competing financial interest.

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