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Copper-Catalyzed Oxidative Cyclization of 1,5-Enynes with Concomitant C−C Bond Cleavage: An Unexpected Access to 3-Formyl-1-indenone Derivatives

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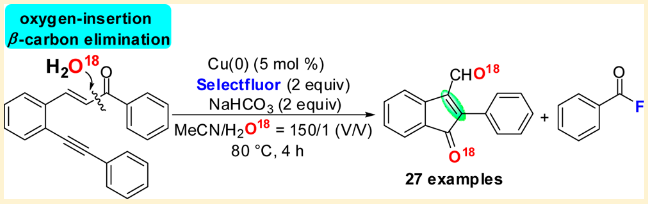
Supporting Information

ABSTRACT: A Cu(0)/Selectfluor system-mediated oxidative cyclization of 1,5-enynes with concomitant C−C bond cleavage to access 3-formyl-1-indenone derivatives is described. Preliminary mechanistic investigations disclosed that the C−C bond cleavage involved a novel water-participated oxygen-insertion *β*-carbon elimination through double oxycuprations.



■ INTRODUCTION

The catalytic and selective cleavage of C−C bonds for chemical transformations remains one of the most challenging tasks in organic synthesis.[1] Over the past few decades, transition-metal-involved C−C bond cleavage has proved to be the most promising tool for this purpose.[1,2] In this context, two elemental reactions, namely oxidative addition[1a,3] and *β*-carbon elimination,[1a,c,d,4] were explored to achieve C−C bond cleavage. Different from the direct insertion of a transition metal into the C−C bond by the oxidative addition process, the *β*-carbon elimination process relies on the formation of a carbon−metal (i.e., M−C−C−C)[5] or heteroatom−metal species (i.e., M−X−C−C, X = O and N).[6−11] In particular, the metal alkoxide-based *β*-carbon eliminations have been increasingly applied in a variety of novel chemical transformations in recent years.[1d,6−10] A range of substrates containing oxyl functionalities, e.g., tertiary alcohols,[2g,i,6] secondary alcohols,[7] *gem*-diols,[8] ketones,[9] and epoxides,[10] are easy to generate metal alkoxides and induce *β*-carbon eliminations (Scheme 1a). On the other hand, we envision that the in situ position of oxyl groups in an unmodified carbon−carbon backbone via tandem reactions may provide an alternative way to achieve the alkoxide-based *β*-carbon elimination. However, such examples have been rarely reported in the literature.[12] Herein, we present an unexpected observation of a water-participated oxygen insertion *β*-carbon elimination in a copper-catalyzed oxidative cyclization of 1,5-enynes in the presence of Selectfluor (Scheme 1b).[12,13]

■ RESULTS AND DISCUSSION

As part of our continued interest in the application of tandem reactions[14] in efficient organic synthesis,[15] we focused on the development of tandem reactions involving the multifold formation and/or cleavage of chemical bonds in a single synthetic step.[15f,g] Recently, we have disclosed that the redox reaction between the Cu(0) powder and Selectfluor in the presence of water enables the generation of FCu(II)BF_4 and/or FCu(II)OH species which can easily undergo oxycupration of alkynes.[16] Considering that enynes[17] are useful precursors for the construction of cyclic compounds upon nucleometalations,[18] we envisioned that the oxycupration of alkynes in 1,5-enyne **1** followed by an insertion of the resulting organocopper species into the C═C bond would result in the formation of a certain cyclic compound, whereby an indenone derivative **2**[19] was unexpectedly obtained involving an unusual water-participated oxygen-insertion *β*-carbon elimination (Scheme 1b). The indenone derivative can serve as a useful synthetic intermediate for natural products, ligand scaffolds, and functional materials.[20]

We commenced the study by treatment of 1,5-enyne **1a** with 5 mol % of Cu(0) powder, 2 equiv of Selectfluor, and $NaHCO_3$ in CH_3CN/H_2O (50/1, v/v) at 80 °C for 4 h, where **2a** was obtained in 43% yield and benzoyl fluoride **3a** was concurrently produced in 29% yield (entry 1, Table 1). Gradually reducing the amount of water in CH_3CN gave better yields of **2a** (60−72%, entries 2−4, Table 1), while using dried CH_3CN gave a low yield of **2a** (entry 5, Table 1), indicating that the reaction is sensitive to the amount of water in the solvent. Through carefully optimization, the combined CH_3CN/H_2O = 150:1 (v/v) solvent system proved to be the best choice of medium for the reaction (entry 3 vs 1, 2, 4−7, Table 1). In addition, the reaction is also sensitive to the base additives. Among several bases examined so far, $NaHCO_3$ proved to be the most suitable base (entry 3 vs 8−11, Table 1). Furthermore, the catalytic activity of a series of copper and gold salts was also evaluated for the reaction. It was found that CuI, $CuSO_4{\cdot}5H_2O$, and $Cu(NO_3)_2{\cdot}3H_2O$ displayed slightly lower catalytic activity than that of Cu(0) (50−63%, entries 12−14 vs 3, Table 1), while other salts showed much lower catalytic activity than that of Cu(0) (entries 15−21 vs 3, Table 1). Selectfluor (2 equiv) was indispensable for the

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Scheme 1. Strategies for Metal Alkoxide-Based β-Carbon Elimination

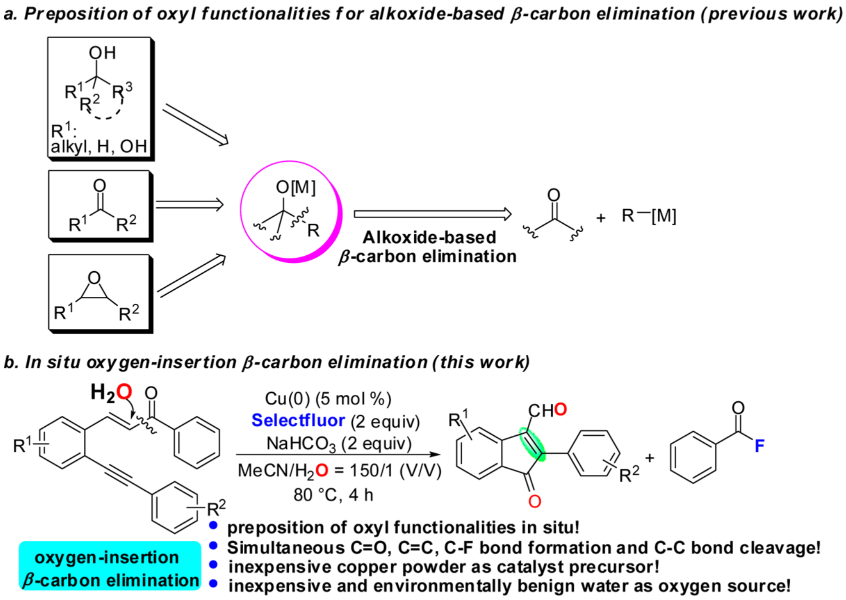
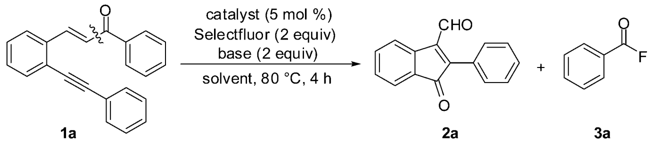


Table 1. Optimization of Reaction Conditions[a]



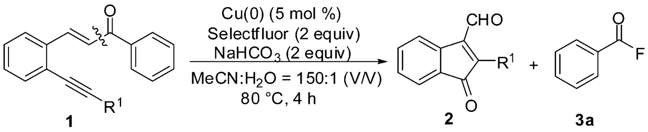
				yield (%)	
entry	catalyst	solvent (v/v)	base	2a	3a
1	Cu	$MeCN/H_2O$ = 50:1	$NaHCO_3$	43	29
2	Cu	$MeCN/H_2$ = 100:1	$NaHCO_3$	60	41
3	**Cu**	**$MeCN/H_2O$ = 150:1**	**$NaHCO_3$**	**72**	**46**
4	Cu	$MeCN/H_2O$ = 200:1	$NaHCO_3$	65	41
5	Cu	MeCN[b]	$NaHCO_3$	<10	
6	Cu	DCM/H_2O = 150:1	$NaHCO_3$	16	
7	Cu	dioxane/H_2O = 150:1	$NaHCO_3$	25	
8	Cu	$MeCN/H_2O$ = 150:1	Na_2CO_3	26	
9	Cu	$MeCN/H_2O$ = 150:1	NaOH	18	
10	Cu	$MeCN/H_2O$ = 150:1	KOH	31	
11	Cu	$MeCN:H_2O$ = 150:1		0	
12	CuI	$MeCN/H_2O$ = 150:1	$NaHCO_3$	63	40
13	$CuSO_4{\cdot}5H_2O$	$MeCN/H_2O$ = 150:1	$NaHCO_3$	60	38
14	$Cu(NO_3)_2{\cdot}3H_2O$	$MeCN:H_2O$ = 150:1	$NaHCO_3$	50	
15	CuBr	$MeCN/H_2O$ = 150:1	$NaHCO_3$	<3	
16	CuCl	$MeCN/H_2O$= 150:1	$NaHCO_3$	<3	
17	$CuCl_2{\cdot}3H_2O$	$MeCN/H_2O$ = 150:1	$NaHCO_3$	30	
18	AuCl	$MeCN/H_2O$ = 150:1	$NaHCO_3$	0	
19	$AuCl_3$	$MeCN/H_2O$ = 150:1	$NaHCO_3$	0	
20	Ph_3PAuCl	$MeCN/H_2O$ = 150:1	$NaHCO_3$	<3	
21	$Ph_3PAuNTf_2$	$MeCN/H_2O$ = 150:1	$NaHCO_3$	<3	
22	Cu	$MeCN/H_2O$ = 150:1	$NaHCO_3$	0,[c] 10,[d,e] 50[d,e]	
23	Cu	$MeCN/H_2O$ = 150:1	$NaHCO_3$	0[f-h], 0[f-h], 0[f-h]	
24		$MeCN/H_2O$ = 150:1	$NaHCO_3$	0	
25	Cu	$MeCN/H_2O$ = 150:1	$NaHCO_3$	56[i]	34

[a] All reactions were carried out with **1a** (0.2 mmol), Cu(0) (5 mol % based on **1a**), Selectfluor (2 equiv), and base (2 equiv) in solvent (2 mL) at 80 °C for 4 h unless otherwise noted. [b] Dried by refluxing with CaH_2. [c] In the absence of Selectfluor. [d,e] In the presence of 0.5 and 1 equiv of Selectfluor, respectively. [f-h] Selectfluor was replaced by 1-fluoro-2,6-dichloropyridinium triflate, 2,6-dichloro-1-fluoropyridinium trifluoromethanesulfonate, and *N*-fluorobenzenesulfonimide, respectively. [i] The reaction temperature is 25 °C, and the reaction time is 12 h.

reaction; otherwise, the yield of **2a** would be reduced (entry 22, Table 1). When Selectfluor was replaced by other F^+ reagents, e.g., 1-fluoro-2,6-dichloropyridinium triflate, 2,6-dichloro-1-fluoropyridinium trifluoromethanesulfonate, or *N*-fluorobenzenesulfonimide, the reaction failed to give the desired product **2a**, while **1a** was recovered quantitatively (entry 23, Table 1). Control experiments showed that no desired product was detected in the absence of a copper powder (entry 24, Table 1). Note that the reaction also took place at room temperature, although a prolonged reaction time was required (entry 25, Table 1).

With optimized reaction conditions in hand, we set out to investigate the effect of the *ortho*-substituted alkyne groups in chalcone **1** on the formation of **2** (Table 2). For substrates bearing aromatic alkyne moieties, the reaction generally proceeded well to furnish 3-formyl-1-indenones **2** in moderate to good yields (54−82%, entries 1−4, 6−13, Table 2) except that (4-ethoxyphenyl)ethynyl-substituted chalcone **1e** gave a complex mixture (entry 5, Table 2). It was found that alkyne moieties bearing electron-deficient aryl rings generally gave better yields of **2** than those substituted with electron-rich ones (entries 6−13 vs 2−4, Table 2). Note that aromatic alkyne moieties bearing substitutents at different positions on the phenyl ring afforded the desired products in similar percent yields (entries 6−8; 9−11; 12 and 13, Table 2). An *n*-hexynyl- and a cyclopropylethynyl-substituted chalcone **1n** and **1o** failed to give the desired products (entries 14 and 15, Table 2).

Table 2. Effect of *Ortho*-Substituted Alkyne Groups in Chalcone 1 on Formation of 2[a]



entry	substrate **1**	product **2**	yield of **2** (%)
1	**1a**: R = Ph	**2a**	72
2	**1b**: R = 2-MeC_6H_4	**2b**	60[b]
3	**1c**: R = 4-MeC_6H_4	**2c**	64[b]
4	**1d**: R = 4-(*n*-C_5H_{11})C_6H_4	**2d**	54[b]
5	**1e**: R = 4-EtOC_6H_4	**2e**	complex mixture
6	**1f**: R = 2-FC_6H_4	**2f**	82
7	**1g**: R = 3-FC_6H_4	**2g**	80
8	**1h**: R = 4-FC_6H_4	**2h**	79
9	**1i**: R = 2-ClC_6H_4	**2i**	71
10	**1j**: R = 3-ClC_6H_4	**2j**	73
11	**1k**: R = 4-ClC_6H_4	**2k**	72
12	**1l**: R = 3-BrC_6H_4	**2l**	72
13	**1m**: R = 4-BrC_6H_4	**2m**	71
14	**1n**: R = *n*-hexyl	**2n**	0
15	**1o**: R = cyclopropyl	**2o**	0

[a] All reactions were carried out with **1** (0.2 mmol), Cu(0) (5 mol % based on **1**), Selectfluor (2 equiv), and $NaHCO_3$ (2 equiv) in solvent (2 mL) at 80 °C for 4 h unless otherwise noted. [b] The starting material could not be completely consumed.

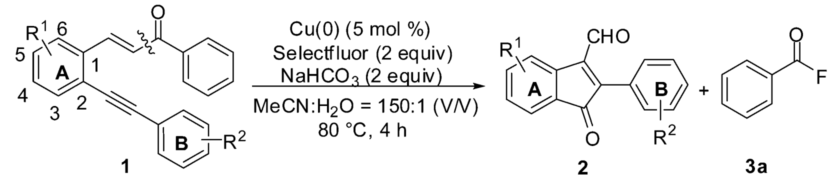
Next, a variety of chalcones **2** with different substituents on both aromatic rings A and B were examined under the standard reaction conditions (Table 3). Substrates bearing both electron-donating (**1p−s,w**) and electron-withdrawing substituents (**1t−v, x−2a**) on the aromatic ring A could be successfully transformed into the desired products in moderate yields (**2p−za**, 60−75%). Note that halo groups on the aromatic ring **A** and **B** were well tolerated under the reaction conditions (**2r−v**, **2x−z**), which could provide opportunities for further functionalizations.

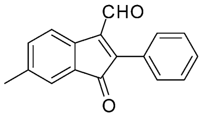
To examine the effect of different acyl groups in the chalcone scaffold on the cleavage of the C−C bond, we synthesized chalcones **1a′**, **1a″**, and **1a‴** (Figure 1). Although chalcones bearing leaving groups such as 4-methylbenzoyl, 4-chlorobenzoyl, and acetyl could also undergo C−C bond cleavage under the optimized reaction conditions, these leaving groups were inferior to benzoyl group as the leaving group (4-methylbenzoyl, 48%; 4-chlorobenzoyl, 40%; acetyl, 35%; benzoyl, 72%; Figure 1 vs entry 3, Table 1) due to the low conversion of the starting materials **1a′**−**1a‴** to the desired products.

Preliminary experiments were done to gain a mechanistic insight into the oxidative cyclization/C−C bond cleavage processes (Scheme 2). When **1a** reacted under the standard reaction conditions except using a CH_3CN/H_2O^{18} = 150:1 (v/v) solvent system, the double-^{18}O-incorporated product $[^{18}O]_2$-**2a** (m/z = 238), mono-^{18}O-incorporated product $[^{18}O]$-**2a** (m/z = 236), and **2a** (m/z = 234), with a molar ratio of 17:48:35, were all detected (see Figure S3, Supporting Information),[21] suggesting that both of the carbonyl oxygen atoms in **2a** originated from water (eq 1). As for the product **3a**, surprisingly, both $[^{16}O]$-**3a** (m/z = 124, see Figure S2, Supporting Information) and the ^{18}O-incorporated product $[^{18}O]$-**3a** (m/z = 126) with a molar ratio of 95:5 were detected in the reaction mixtures (eq 1, see Figure S4, Supporting Information). When the preparative *o*-alkynyl expoxide **4** was subjected to the standard conditions, **2a** could also be obtained in 60% yield, indicating that **4** was likely an intermediate for the reaction (eq 2). Over the course of the reaction, we could not detect the existence of **4**, probably due to the fast conversion of **4** to **2a**. Fortunately, when a chalcone **5** not containing an alkyne moiety was subjected to the standard reaction conditions, an epoxide product **6** was indeed isolated in 88% yield and the ^{18}O-labeling experiment unambiguously established that the oxygen atom of the epoxide **6** originated from water (eq 3, see Figure S6, Supporting Information). The reaction gave a decreased yield of **2a** (65%) in the presence of 0.2 equiv of TEMPO and failed to give **2a** by using 3 equiv of TEMPO (eq 4), demonstrating that the reaction may involve a radical process.[22]

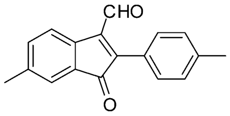
Consequently, a proposed mechanism was depicted in Scheme 3. First, the redox reaction between copper powder and Selectfluor may produce a cationic copper species $FCu(II)BF_4$ **7** and release a base **8**.[16,23] Then activation of the C═C moiety of **1a** by **7** followed by the nucleophilic addition of H_2O^{18} to the C═C bond and the abstraction of a proton by the base **8** resulted in the formation of intermediates **9** and **11**.[16,18a] On the other hand, in our previous work,[16] we have disclosed that **7** may be transferred into a copper species **10** in the presence of H_2O^{18} under the basic conditions. Thus, an oxycupration of the C═C bond in **1a** by **10** via an inner-sphere model could alternatively generate the intermediate **11**.[16] Compound **11** could be transferred into **12** under the basic conditions. Subsequently, **12** underwent reductive elimination to give an epoxide intermediate $[\mathbf{O^{18}}]$-**4**.[24] An oxycupration of the triple bond in $[\mathbf{O^{18}}]$-**4** by **7** and/or **10** followed by a ring-opening of the epoxide moiety in **13** gave an intermediate **14**.[16] Compound **14** underwent the alkoxide-based *β*-carbon elimination to deliver an intermediate **15** and benzoyl fluoride **3a**. This alkoxide-based *β*-carbon elimination may also proceed via a radical process in the presence of Selectfluor.[25] Finally, the aromatization of **15** under oxidative conditions gave $[\mathbf{O^{18}}]_2$-**2a**.[13a] On the other hand, **14** may also be isomerized into **18** via an oxygen-exchanging process. Compound **18** underwent the *β*-carbon elimination in the presence of Selectfluor and could thus give products $[\mathbf{O^{18}}]$-**2a** and $[\mathbf{O^{18}}]$-**3a**. In addition, a reaction pathway to **2a** involving the formation of an intermediate **19** could not be completely excluded.

Table 3. Formation of 2 from Various Substituted *o*-Alkynyl Chalcone 1[a]

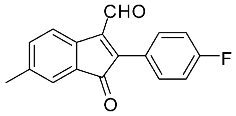




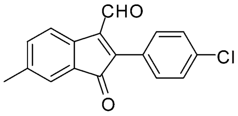
2p (72%)



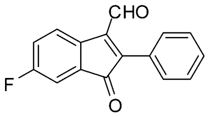
2q (75%)



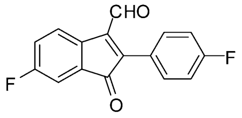
2r (68%)



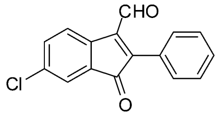
2s (73%)



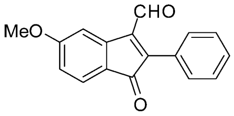
2t (67%)



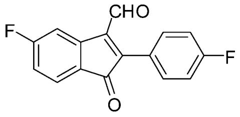
2u (73%)



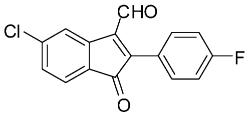
2v (60%)



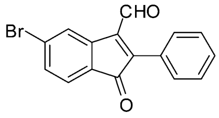
2w (66%)



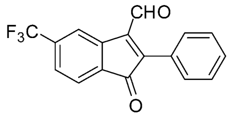
2x (66%)



2y (69%)



2z (63%)



2za (68%)

[a]All reactions were carried out with **1** (0.2 mmol), Cu(0) (5 mol % based on **1**), Selectfluor (2 equiv), and $NaHCO_3$ (2 equiv) in solvent (2 mL) at 80 °C for 4 h unless otherwise noted.

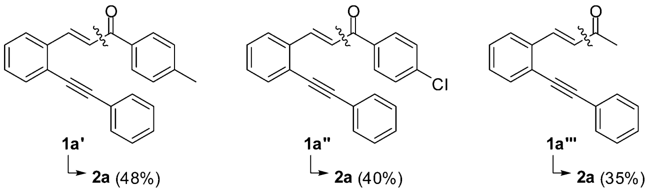


Figure 1. Effect of acyl groups on the cleavage of the C−C bond to produce **2a** under the standard reaction conditions.

■ CONCLUSION

In summary, we have described an unusual copper-catalyzed oxidative cyclization of 1,5-enynes with concomitant C−C bond cleavage. The present procedure enabled simultaneous formation of one C−C, one C−F, and two C═O bonds as well as cleavage of one C−C bond merely in a single synthetic step by a single copper catalyst. To the best of our knowledge, this is the first example of water-participated oxygen-insertion *β*-carbon elimination and the oxidative cleavage of a single C−C bond into a C═O and a C−F bond.[12,13] In addition, the application of this copper-catalyzed oxygen-insertion *β*-carbon elimination in other organic synthesis is currently underway in our laboratory.

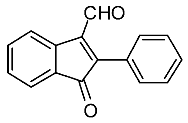
■ EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purifications. Melting points are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a spectrometer at 25 °C in $CDCl_3$ at 500 MHz, 125 MHz, respectively, with TMS as internal standard. ^{19}F NMR spectra were recorded on a spectrometer at 25 °C in $CDCl_3$ at 376 MHz, with CF_3COOH as external standard. Chemical shifts (δ) are expressed in ppm and coupling constants J are given in Hz. The IR spectra were recorded on an FT-IR spectrometer. GC−MS experiments were performed with EI source; high-resolution mass spectra (HRMS) were obtained on a TOF MS instrument with EI source.

Starting Materials. The starting material 1,5-enynes **1** were synthesized according to the literature procedures.[26]

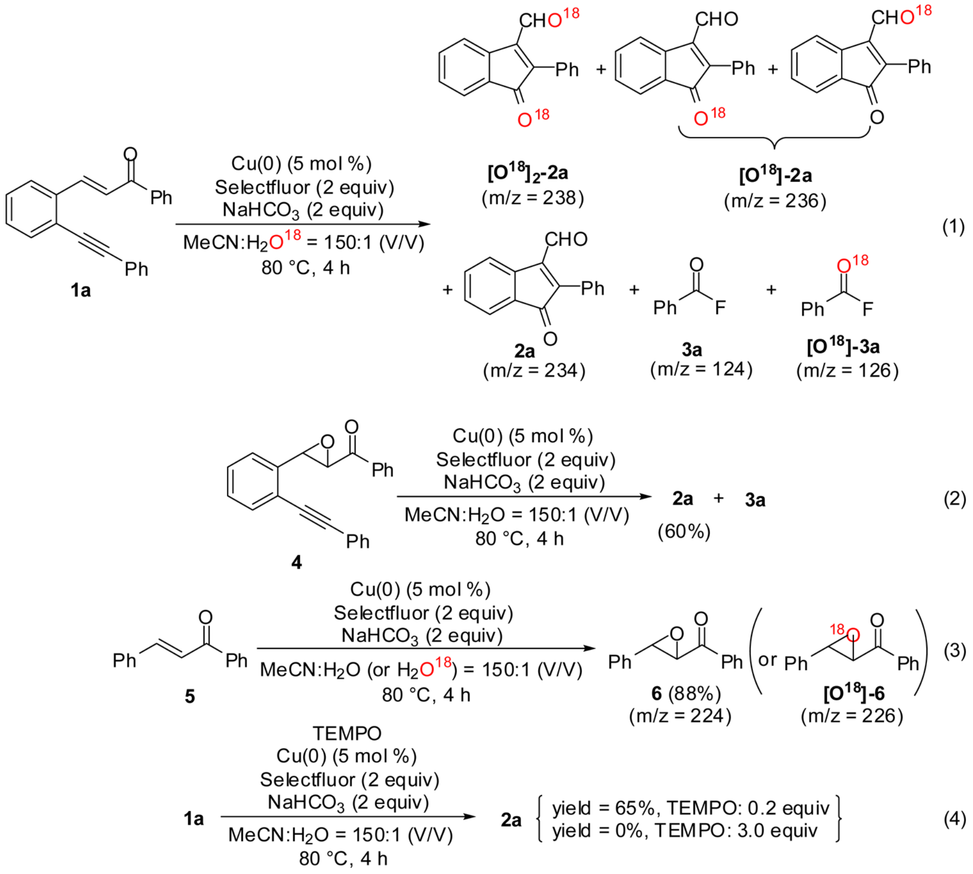
Typical Experimental Procedure for the Synthesis of 3-Formyl-1-indenones 2 from 1. Compound **1** (0.2 mmol), Cu(0) powder (0.64 mg, 5 mol %), Selectfluor (141.7 mg, 0.4 mmol, 2 equiv), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2 equiv), and CH_3CN/H_2O = 150:1 (v/v, 2 mL) were added to a 10 mL flask. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether/EtOAc (10/1, v/v) as the eluent to give pure **2**.

*1-Oxo-2-phenyl-1H-indene-3-carbaldehyde (**2a**):*[19a]

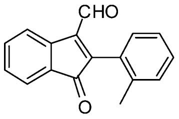


orange solid (33.7 mg, 72%); R_f = 0.48 (petroleum ether/EtOAc, 6:1); mp 155.6−156.9 °C; IR (neat, cm^{-1}): ν = 1722 (C═O); ^{1}H NMR ($CDCl_3$, 500 MHz) 10.33 (s, 1H), 8.01 (d, J = 7.0 Hz, 1H), 7.65 (d, J = 7.0 Hz, 1H), 7.57−7.49 (m, 6H), 7.36−7.33 (m, 1H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 125 MHz) δ 196.9, 191.0, 145.0, 143.7, 142.3, 134.7, 130.7, 130.5, 129.5, 129.3, 128.7, 128.1, 124.23, 124.17; GC−MS (EI, 70 eV) m/z = 234 (100) [M^+].

Scheme 2. Preliminary Mechanistic Studies

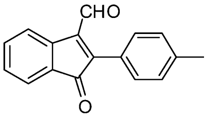


1-Oxo-2-o-tolyl-1H-indene-3-carbaldehyde (**2b**):



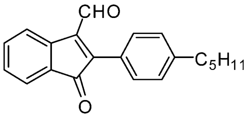
orange solid (29.8 mg, 60%); R_f = 0.47 (petroleum ether/EtOAc, 6:1); mp 175−180 °C; IR (neat, cm^{-1}) ν = 1722 (C═O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.08 (s, 1H), 8.00 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.51−7.23 (m, 6H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 196.5, 190.8, 148.2, 145.1, 142.1, 137.5, 134.5, 130.9, 130.8, 130.0, 129.8, 129.3, 127.9, 125.8, 124.3, 124.2, 20.7; GC−MS (EI, 70 eV) m/z = 248 (100) [M$^+$]; HRMS (EI) for $C_{17}H_{12}O_2$ calcd 248.0837, found 248.0843.

1-Oxo-2-p-tolyl-1H-indene-3-carbaldehyde (**2c**):



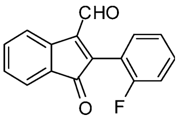
orange solid (31.8 mg, 64%); R_f = 0.49 (petroleum ether/EtOAc, 6:1); mp 123−127 °C; IR (neat, cm^{-1}): ν = 1714 (C═O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.32 (s, 1H); 8.00 (d, J = 7.5 Hz, 2H), 7.64 (d, J = 7.0 Hz, 1H), 7.49−7.33 (m, 6H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 197.2, 191.1, 145.2, 143.1, 141.2, 134.7, 130.7, 129.7, 129.5, 129.1, 128.8, 125.4, 124.2, 124.1, 21.6; GC−MS (EI, 70 eV) m/z = 248 (100) [M$^+$]; HRMS (EI) for $C_{17}H_{12}O_2$ calcd 248.0837, found 248.0841.

1-Oxo-2-(4-pentylphenyl)-1H-indene-3-carbaldehyde (**2d**):



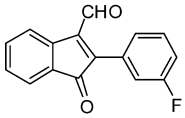
orange solid (32.9 mg, 54%); R_f = 0.50 (petroleum ether/EtOAc, 6:1); mp 58−63 °C; IR (neat, cm^{-1}) ν =1720 (C═O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.33 (s, 1H), 8.0 (d, J = 7.0 Hz, 1H), 7.64 (d, J = 7.5 Hz, 1H), 7.50−7.32 (m, 6H), 2.69 (t, J = 7.5 Hz, 2H), 1.68 (m, 2H), 1.38−1.35 (m, 4H), 0.93 (t, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 197.2, 191.2, 146.2, 145.2, 143.1, 142.6, 134.7, 130.7, 129.6, 129.1, 128.9, 125.6, 124.2, 124.1, 36.0, 31.5, 30.9, 22.5, 14.0; GC−MS (EI, 70 eV) m/z = 304 (100) [M$^+$]; HRMS (EI) for $C_{21}H_{20}O_2$ calcd 304.1463, found 304.1456.

2-(2-Fluorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2f**):



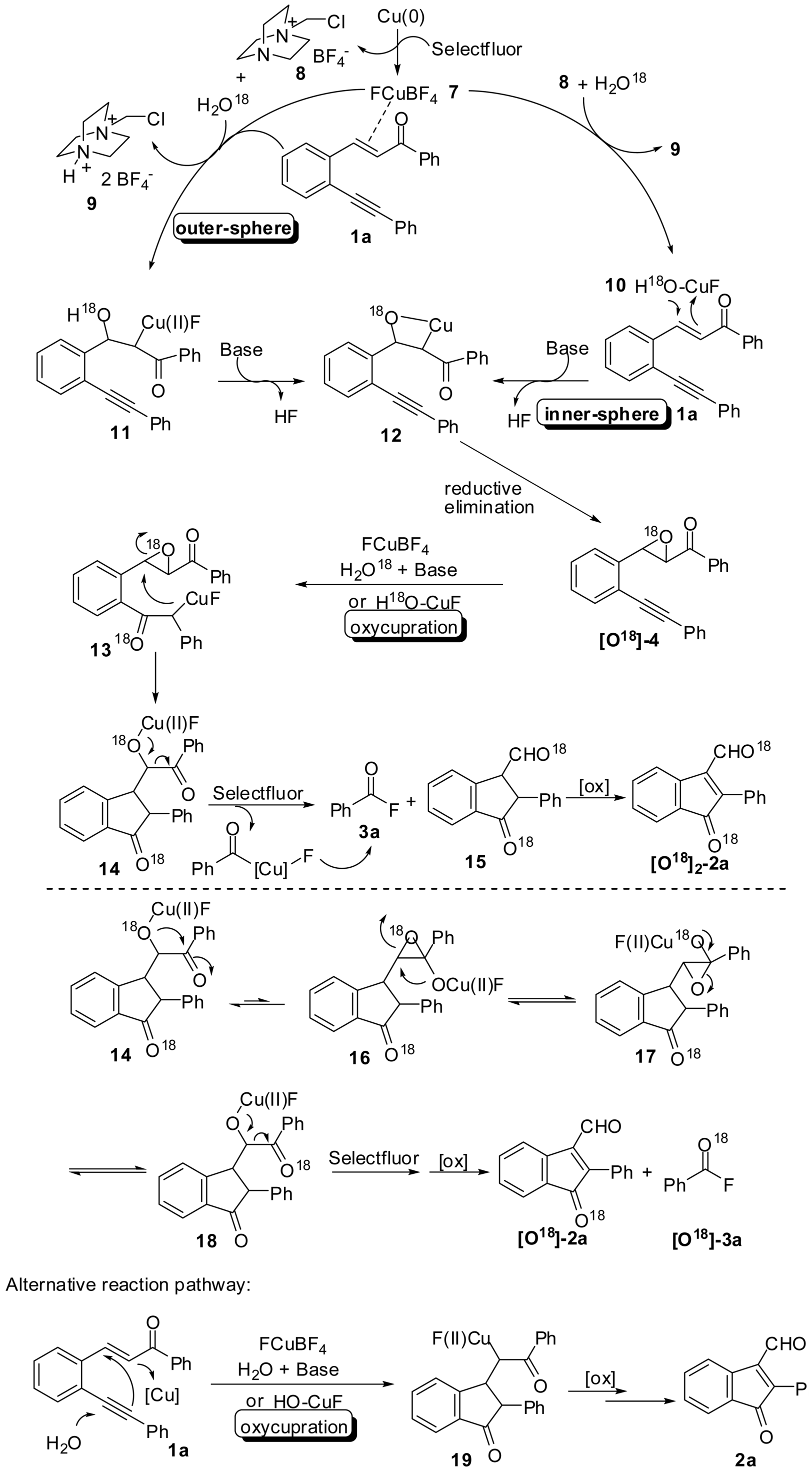
orange solid (41.4 mg, 82%); R_f = 0.47 (petroleum ether/EtOAc, 6:1); mp 150−154 °C; IR (neat, cm^{-1}) ν =1716 (C═O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.24 (d, J = 4.0 Hz, 1H), 8.0 (d, J = 7.5 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.52−7.22 (m, 6H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 195.6, 190.2 (d, J = 5.0 Hz), 160.6 (d, J = 247.5 Hz), 145.0, 142.0, 139.0, 134.5, 132.3, 131.9 (d, J = 8.8 Hz), 129.9, 129.5, 124.42, 124.38, (d. J = 3.8 Hz), 124.2, 116.4 (d. J = 15.0 Hz), 116.2 (d. J = 21.3 Hz); ^{19}F NMR (CDCl$_3$, 376 MHz) δ −112.7; GC−MS (EI, 70 eV) m/z = 252 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9FO_2$ calcd 252.0587, found 252.0594.

2-(3-Fluorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2g**):



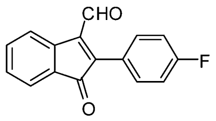
orange solid (40.4 mg, 80%); R_f = 0.48 (petroleum ether/EtOAc, 6:1); mp 107−113 °C; IR (neat, cm^{-1}) ν = 1717 (C═O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.34 (s, 1H), 8.0 (d, J = 7.5 Hz, 1H), 7.65 (d, J = 7.0 Hz, 1H), 7.52−7.24 (m, 6H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 196.3, 190.5, 162.7 (d, J = 246.3 Hz), 144.4, 143.4, 142.0, 134.8, 130.4 (d, J = 8.8 Hz), 130.1 (d, J = 7.5 Hz), 129.7, 129.5, 126.5

Scheme 3. Proposed Mechanism



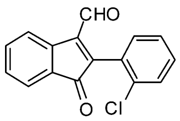
(d, J = 3.8 Hz), 124.44, 124.41, 117.6, 117.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −112.0; GC−MS (EI, 70 eV) m/z = 252 (100) [M^+]; HRMS (EI) for $C_{16}H_9FO_2$ calcd 252.0587, found 252.0591.

*2-(4-Fluorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2h**):*



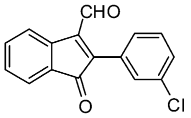
orange solid (39.8 mg, 79%); R_f = 0.47 (petroleum ether/EtOAc, 6:1); mp 150−154 °C; IR (neat, cm^{-1}) ν = 1715 (C═O); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.31 (s, 1H), 7.99 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 7.0 Hz, 1H), 7.58−7.21 (m, 6H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 196.8, 190.6, 164.3 (d, J = 251.3 Hz), 143.8, 143.5, 142.2, 134.8, 132.7 (d, J = 8.8 Hz), 129.4, 124.34, 124.30, 124.28, 124.24, 116.1 (d, J = 22.5 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −109.0; GC−MS (EI, 70 eV) m/z = 252 (100) [M^+]; HRMS (EI) for $C_{16}H_9FO_2$ calcd 252.0587, found 252.0593.

*2-(2-Chlorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2i**):*



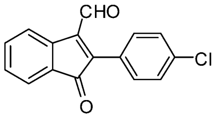
orange solid (38.2 mg, 71%), R_f = 0.50 (petroleum ether/EtOAc, 6:1); mp 142−150 °C; IR (neat, cm^{-1}) ν = 1714 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.33 (s, 1H), 8.0 (d, J = 7.5 Hz, 1H), 7.66 (d, J = 7.0 Hz, 1H), 7.56−7.35 (m, 6H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 196.2, 190.4, 144.5, 143.3, 142.0, 134.9, 134.8, 130.5, 130.4, 130.0, 129.9, 129.6, 129.5, 128.8, 124.5, 124.4; GC−MS (EI, 70 eV) m/z = 268 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9ClO_2$ calcd 268.0291, found 268.0287.

*2-(3-Chlorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2j**):*



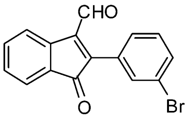
orange solid (39.2 mg, 73%), R_f = 0.51 (petroleum ether/EtOAc, 6:1); mp 98−105 °C; IR (neat, cm^{-1}) ν = 1723 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.14 (s, 1H), 8.01 (d, J = 7.0 Hz, 1H), 7.65 (d, J = 7.0 Hz, 1H), 7.56−7.34 (m, 6H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 195.5, 190.2, 145.6, 143.9, 141.7, 134.6, 134.2, 132.1, 131.1, 130.3, 129.8, 129.7, 127.7, 126.8, 124.6, 124.4; GC−MS (EI, 70 eV) m/z = 268 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9ClO_2$ calcd 268.0291, found 268.0295.

*2-(4-Chlorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2k**):*



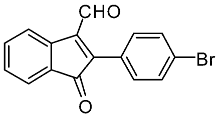
red solid (38.7 mg, 72%); R_f = 0.53 (petroleum ether/EtOAc, 6:1); mp 145−150 °C; IR (neat, cm^{-1}) ν = 1717 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.31 (s, 1H), 8.0 (d, J = 7.5 Hz, 1H), 7.65 (d, J = 7.0 Hz, 1H), 7.51−7.34 (m, 6H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 196.5, 190.4, 143.9, 143.6, 142.1, 137.1, 134.8, 131.9, 129.53, 129.45, 129.2, 126.6, 124.4, 124.3; GC−MS (EI, 70 eV) m/z = 268 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9ClO_2$ calcd 268.0291, found 268.0294.

*2-(3-Bromophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2l**):*



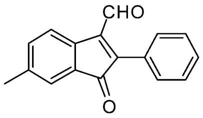
red solid (45.1 mg, 72%); R_f = 0.53 (petroleum ether/EtOAc, 6:1); mp 125−129 °C; IR (neat, cm^{-1}) ν = 1720 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.31 (s, 1H), 7.99 (d, J = 7.5 Hz, 1H), 7.67−7.33 (m, 7H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 196.4, 190.4, 143.9, 143.6, 142.1, 134.8, 134.5, 132.1, 132.0, 129.5, 129.4, 127.4, 127.0, 125.4, 124.34, 124.31; GC−MS (EI, 70 eV) m/z = 312 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9BrO_2$ calcd 311.9786, found 311.9792.

*2-(4-Bromophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2m**):*



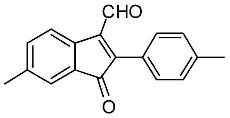
red solid (44.5 mg, 71%); R_f = 0.54 (petroleum ether/EtOAc, 6:1); mp 128−132 °C; IR (neat, cm^{-1}) ν = 1717 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.31 (s, 1H), 8.0 (d, J = 7.5 Hz, 1H), 7.68−7.34 (m, 7H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 197.2, 190.8, 144.1, 143.6, 142.3, 135.1, 132.1, 132.0, 129.7, 129.6, 127.2, 125.6, 124.64, 124.55; GC−MS (EI, 70 eV) m/z = 312 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9BrO_2$ calcd 311.9786, found 311.9790.

*6-Methyl-1-oxo-2-phenyl-1H-indene-3-carbaldehyde (**2p**):*



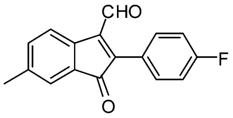
red solid (35.8 mg, 72%); R_f = 0.46 (petroleum ether/EtOAc, 6:1); mp 125−130 °C; IR (neat, cm^{-1}) ν = 1715 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.30 (s, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.56−7.29 (m, 7H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 197.2, 191.1, 144.5, 144.0, 139.7, 139.5, 134.8, 130.6, 130.3, 129.9, 128.7, 128.3, 125.2, 124.0, 21.3; GC−MS (EI, 70 eV) m/z = 248 (100) [M$^+$]; HRMS (EI) for $C_{17}H_{12}O_2$ calcd 248.0837, found 248.0834.

*6-Methyl-1-oxo-2-p-tolyl-1H-indene-3-carbaldehyde (**2q**):*



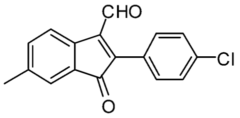
red solid (39.3 mg, 75%); R_f = 0.53 (petroleum ether/EtOAc, 6:1); mp 100−108 °C; IR (neat, cm^{-1}) ν = 1718 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.30 (s, 1H); 7.85 (d, J = 7.5 Hz, 1H), 7.46−7.27 (m, 6H), 2.45 (s, 3H), 2.39 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 197.5, 191.1, 144.6, 143.3, 140.9, 139.7, 139.4, 134.7, 130.6, 129.9, 129.5, 125.5, 125.1, 123.8, 21.5, 21.3; GC−MS (EI, 70 eV) m/z = 262 (100) [M$^+$]; HRMS (EI) for $C_{18}H_{14}O_2$ calcd 262.0994, found 262.0986.

*2-(4-Fluorophenyl)-6-methyl-1-oxo-1H-indene-3-carbaldehyde (**2r**):*



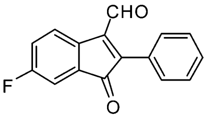
red solid (36.2 mg, 68%); R_f = 0.45 (petroleum ether/EtOAc, 6:1); mp 158−163 °C; IR (neat, cm^{-1}) ν = 1719 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.29 (s, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.56−7.54 (m, 2H), 7.46 (s, 1H), 7.29−7.20 (m, 3H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 197.1, 190.6, 164.1 (d, J = 251.3 Hz), 143.8, 143.2, 139.8, 139.4, 134.9, 132.6 (d, J = 8.8 Hz), 129.7, 125.2, 124.4 (d, J = 2.5 Hz), 124.0, 116.0 (d, J = 22.5 Hz), 21.3; ^{19}F NMR (CDCl$_3$, 376 MHz) δ −109.4; GC−MS (EI, 70 eV) m/z = 266 (100) [M$^+$]; HRMS (EI) for $C_{17}H_{11}FO_2$ calcd 266.0743, found 266.0750.

*2-(4-Chlorophenyl)-6-methyl-1-oxo-1H-indene-3-carbaldehyde (**2s**):*



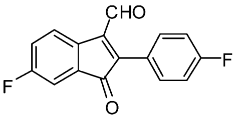
red solid (41.3 mg, 73%); R_f = 0.44 (petroleum ether/EtOAc, 6:1); mp 155−159 °C; IR (neat, cm^{-1}) ν = 1719 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.29 (s, 1H); 7.85 (d, J = 7.5 Hz, 1H), 7.49 (s, 4H), 7.45 (s, 1H), 7.29 (d, J = 8.0 Hz, 1H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 196.8, 190.5, 144.2, 143.0, 139.9, 139.3, 136.8, 134.9, 131.8, 129.1, 126.7, 125.3, 124.1, 21.4; GC−MS (EI, 70 eV) m/z = 282 (100) [M$^+$]; HRMS (EI) for $C_{17}H_{11}ClO_2$ calcd 282.0448, found 282.0452.

*6-Fluoro-1-oxo-2-phenyl-1H-indene-3-carbaldehyde (**2t**):*



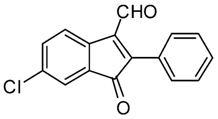
orange solid (33.8 mg, 67%); R_f = 0.52 (petroleum ether/EtOAc, 6:1); mp 130−133 °C; IR (neat, cm^{-1}) ν = 1723 (C=O); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 10.31 (s, 1H), 7.99 (dd, J_1 = 8.0 Hz, J_2 = 4.5 Hz, 1H), 7.56−7.53 (m, 5H), 7.35−7.34 (m, 1H), 7.18−7.14 (m, 1H); ^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$) δ 195.7, 190.8, 163.7 (d, J = 250 Hz), 145.1 (d, J = 3.8 Hz), 143.4, 137.9 (d, J = 3.8 Hz), 131.8 (d, J = 7.5 Hz), 130.7, 130.6, 128.8, 127.9, 125.5 (d, J = 8.8 Hz), 120.2 (d, J = 21.3 Hz), 112.4 (d, J = 25.0 Hz); ^{19}F NMR (CDCl$_3$, 376 MHz) δ −110.9; GC−MS (EI, 70 eV) m/z = 252 (100) [M$^+$]; HRMS (EI) for $C_{16}H_9FO_2$ calcd 252.0587, found 252.0584.

*6-Fluoro-2-(4-fluorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2u**):*



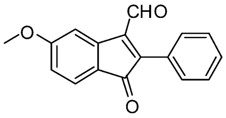
yellow solid (39.4 mg, 73%); R_f = 0.50 (petroleum ether/EtOAc, 6:1); mp 175−180 °C; IR (neat, cm^{-1}) ν = 1718 (C=O); ^{1}HNMR (CDCl$_3$,500 MHz) δ 10.30 (s, 1H), 7.99 (dd, J_1 = 8.0 Hz, J_2 = 4.5 Hz, 1H), 7.57−7.15 (m, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 195.5, 190.3, 164.3 (d, *J* = 251.3 Hz), 163.7 (d, *J* = 250 Hz), 143.7 (d, *J* = 3.8 Hz), 143.2, 137.7 (d, *J* = 3.8 Hz), 132.6 (d, *J* = 8.8 Hz), 125.6 (d, *J* = 7.5 Hz), 124.0 (d, *J* = 2.5 Hz), 120.3 (d, *J* = 22.5 Hz), 116.2 (d, *J* = 21.5 Hz), 112.5, 112.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −108.8, −110.7; GC−MS (EI, 70 eV) *m*/*z* = 270 [M^+]; HRMS (EI) for $C_{16}H_8F_2O_2$ calcd 270.0492, found 270.0498.

*6-Chloro-1-oxo-2-phenyl-1H-indene-3-carbaldehyde (**2v**):*



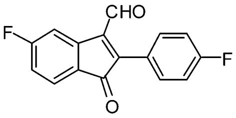
orange oil (32.2 mg, 60%); R_f = 0.45 (petroleum ether/EtOAc, 10:1); IR (neat, cm^{-1}) ν = 1721 (C═O); ^1H NMR ($CDCl_3$, 500 MHz) δ 10.32 (s, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.61−7.46 (m, 7H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 195.7, 190.7, 144.8, 143.3, 140.4, 135.6, 134.0, 131.7, 130.8, 130.7, 128.9, 128.6, 125.2, 124.7; GC−MS (EI, 70 eV) *m*/*z* = 268 (100) [M^+]; HRMS (EI) for $C_{16}H_9ClO_2$ calcd 268.0291, found 268.0287.

*5-Methoxy-1-oxo-2-phenyl-1H-indene-3-carbaldehyde (**2w**):*



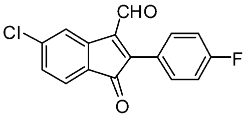
red solid (34.9 mg, 66%); R_f = 0.45 (petroleum ether/EtOAc, 6:1); mp 158−163 °C; IR (neat, cm^{-1}) ν = 1719 (C═O); ^1H NMR ($CDCl_3$, 500 MHz) δ 10.28 (s, 1H), 7.62−7.52 (m, 7H), 6.75 (dd, J_1 = 8.0 Hz, J_2 = 2.5 Hz, 2H), 3.94 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 197.1, 190.9, 168.8, 152.0, 151.9, 140.1, 134.8, 130.6, 130.3, 129.0, 128.7, 127.8, 113.5, 112.5, 59.1; GC−MS (EI, 70 eV) *m*/*z* = 264 (100) [M^+]; HRMS (EI) for $C_{17}H_{12}O_3$ calcd 264.0786, found 264.0792.

*5-Fluoro-2-(4-fluorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2x**):*



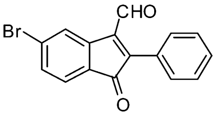
orange solid (35.7 mg, 66%); R_f = 0.51 (petroleum ether/EtOAc, 6:1); mp 144−146 °C; IR (neat, cm^{-1}) ν = 1718 (C═O); ^1H NMR ($CDCl_3$, 500 MHz) δ 10.29 (s, 1H), 7.75 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H), 7.66−7.56 (m, 3H), 7.26−7.22 (m, 2H), 7.01−6.98 (m, 1H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 194.8, 190.0, 166.8 (d, *J* = 255 Hz), 164.5 (d, *J* = 251.3 Hz), 145.4 (d, *J* = 10 Hz), 144.9, 141.6, 132.8 (d, *J* = 7.5 Hz), 126.3 (d, *J* = 10 Hz), 125.3 (d, *J* = 2.5 Hz), 124.0 (d, *J* = 3.8 Hz), 116.3 (d, *J* = 21.3 Hz), 115.4 (d, *J* = 22.5 Hz), 113.1 (d, *J* = 26.3 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −101.1, −108.3; GC−MS (EI, 70 eV) *m*/*z* = 270 (100) [M^+]; HRMS (EI) for $C_{16}H_8F_2O_2$ calcd 270.0492, found 270.0487.

*5-Chloro-2-(4-fluorophenyl)-1-oxo-1H-indene-3-carbaldehyde (**2y**):*



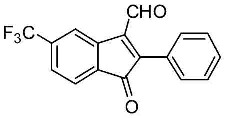
orange solid (39.6 mg, 69%); R_f = 0.49 (petroleum ether/EtOAc, 6:1); mp 150−155 °C; IR (neat, cm^{-1}) ν = 1716 (C═O); ^1H NMR ($CDCl_3$, 500 MHz) δ 10.29 (s, 1H), 8.03 (d, *J* = 1.5 Hz, 1H), 7.59−7.22 (m, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 195.2, 190.0, 164.5 (d, *J* = 252.5 Hz), 144.6, 143.9, 142.3, 141.2, 132.8 (d, *J* = 8.8 Hz), 129.2, 127.5, 125.1, 125.0, 124.0 (d, *J* = 2.5 Hz), 116.3 (d, *J* = 22.5 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −108.3; GC−MS (EI, 70 eV) *m*/*z* = 286 (100) [M^+]; HRMS (EI) for $C_{16}H_8ClFO_2$ calcd 286.0197, found 286.0189.

*5-Bromo-2-phenyl-1-oxo-1H-indene-3-carbaldehyde (**2z**):*



reddish yellow solid (39.5 mg, 63%); R_f = 0.49 (petroleum ether/EtOAc, 10:1); mp 163−165 °C; IR (neat, cm^{-1}) ν = 1721 (C═O); ^1H NMR ($CDCl_3$, 500 MHz) δ 10.30 (s, 1H), 8.21 (s, 1H), 7.56−7.51 (m, 7H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 195.6, 190.5, 145.8, 144.0, 142.5, 132.2, 130.9, 130.8, 129.8, 128.9, 128.2, 127.8, 127.7, 125.2; GC−MS (EI, 70 eV) *m*/*z* = 312 (100) [M^+]; HRMS (EI) for $C_{16}H_9BrO_2$ calcd 311.9786, found 311.9792.

*5-(Trifluoromethyl)-2-phenyl-1-oxo-1H-indene-3-carbaldehyde (**2za**:).*

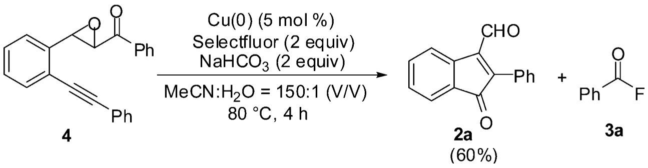


Reddish orange solid (41.1 mg, 68%), R_f = 0.44 (petroleum ether/EtOAc, 10:1); mp 175−177 °C; IR (neat, cm^{-1}) ν = 1726 (C═O); ^1H NMR ($CDCl_3$, 500 MHz) δ 10.36 (s, 1H), 8.30 (s, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.59−7.56 (m, 5H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 195.8, 190.5, 145.5, 143.0, 142.7, 136.1 (*J* = 32.5 Hz), 132.1, 131.0, 130.8, 128.9, 127.6, 126.8 (*J* = 3.8 Hz), 124.1, 123.4 (*J* = 271.3 Hz), 121.0 (*J* = 3.8 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ −64.1; GC−MS (EI, 70 eV) *m*/*z* = 302 (100) [M^+]; HRMS (EI) for $C_{17}H_9F_3O_2$ calcd 302.0555, found 302.0561.

Mechanistic Studies. *Reaction of **1a** in $CH_3CN–H_2O^{18}$ (150:1, v/v) vs in $CH_3CN–H_2O$ (150:1, v/v). Procedure A.* **1a** (61.7 mg, 0.2 mmol), Cu(0) powder (0.64 mg, 5 mol %), Selectfluor (141.7 mg, 0.4 mmol, 2 equiv), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2 equiv), and $CH_3CN:H_2O$ = 150:1 (v/v, 2 mL) were added to a 10 mL flask. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion, the resulting mixture was sampled for GC−MS analysis (see Figures S1 and S2, Supporting Information).

Procedure B. **1a** (61.7 mg, 0.2 mmol), Cu(0) powder (0.64 mg, 5 mol %), Selectfluor (141.7 mg, 0.4 mmol, 2 equiv), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2 equiv), and $CH_3CN:H_2O^{18}$ = 150:1 (v/v, 2 mL) were added to a 10 mL flask. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion, the resulting mixture was sampled for GC−MS analysis (see Figures S3 and S4, Supporting Information).

*Reaction of **4** under the Standard Reaction Conditions.*

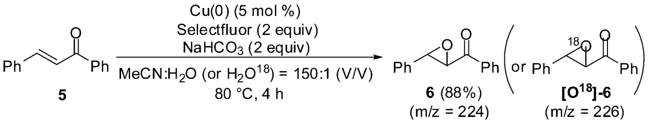


Compound **4** was prepared according to a modified procedure of a reported literature.[27] Procedure: (*E*)-1-phenyl-3-(2-(phenylethynyl)-phenyl)prop-2-en-1-one **1a** (92.5 mg, 0.3 mmol) and THF (2 mL) were added to a screw vial equipped with a magnetic stirring bar. Urea hydrogenperoxide (31 mg, 0.33 mmol) and DBU (11.3 μL, 1.68 mmol) were added at 0 °C, and the mixture was gradually warmed to room temperature. After being stirred for 24 h, the reaction mixture was diluted with AcOEt and washed with saturated aqueous $Na_2S_2O_3$. Then the organic layer was evaporated to give an oily residue, which was purified by silica gel column chromatography (petroleum ether/EtOAc, 6:1, v/v) to afford **4** as a white solid (77.9 mg, 80% yield).

*Analytical data for **4**:* white solid; R_f = 0.55 (petroleum ether/EtOAc, 6:1); mp 95−100 °C; IR (neat, cm^{-1}) ν = 3010, 1651, 1490, 1305, 990, 800, 755, 570; ^1H NMR (500 MHz, $CDCl_3$) δ 8.09−8.08 (m, 2H), 7.59−7.12 (m, 12H), 4.60 (d, *J* = 2.0 Hz, 1H), 4.27 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.2, 139.9, 137.5, 135.3, 133.9, 131.9, 131.4, 128.8, 128.5, 128.42, 128.39, 128.2, 124.2, 122.4, 95.2, 85.9, 58.4 (2C); GC−MS (EI, 70 eV) *m*/*z* = 324(100) [M^+]; HRMS (EI) for $C_{23}H_{16}O_2$ calcd 324.1150, found 324.1156.

*Reaction of **4** under the Standard Reaction Conditions.* Compound **4** (64.9 mg, 0.2 mmol), Cu(0) powder (0.64 mg, 5 mol %), Selectfluor (141.7 mg, 0.4 mmol, 2 equiv), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2 equiv), and CH_3CN/H_2O = 150:1 (v/v, 2 mL) were added to a 10 mL flask. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether/EtOAc (10/1, v/v) as eluent to give pure **2a** (28.1 mg, 60% yield).

*Reaction of **5** under the Standard Reaction Conditions and ^{18}O-Labeling Experiment.*



Procedure: chalcone **5** (41.7 mg, 0.2 mmol), Cu(0) powder (0.64 mg, 5 mol %), Selectfluor (141.7 mg, 0.4 mmol, 2 equiv), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2 equiv), and CH_3CN/H_2O = 150:1 (v/v, 2 mL) were added to a 10 mL flask. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether/EtOAc (8/1, v/v) as eluent to give pure **6** in 88% yield. Using CH_3CN/H_2O^{18} = 150:1 (v/v) as a medium under otherwise identical conditions as the above procedure, the ^{18}O-incorporated product **[O^{18}]-6** was obtained. The GC−MS spectra of **6** and **[O^{18}]-6** are shown in Figure S5, Supporting Information.

*Analytical data of **6**:* white solid (39.4 mg, 88%); R_f = 0.55 (petroleum ether/EtOAc, 8:1); mp 88−89 °C; IR (neat, cm^{-1}) ν = 1690 (C═O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J_1 = 7.5 Hz, J_2 = 0.5 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 8.0 Hz, 2H), 7.43−7.39 (m, 5H), 4.32 (d, J = 2.0 Hz, 1H), 4.10 (d, J = 2.0 Hz, 1H); GC−MS (EI, 70 eV) m/z = 224(10) [M$^+$].

Effect of Radical Scavenger TEMPO on the Model Reaction. Procedure 1a (61.7 mg, 0.2 mmol), Cu(0) powder (0.64 mg, 5 mol %), Selectfluor (141.7 mg, 0.4 mmol, 2 equiv), $NaHCO_3$ (33.6 mg, 0.4 mmol, 2 equiv), TEMPO (6.25 mg, 0.2 equiv; or 93.8 mg, 3 equiv), and CH_3CN/H_2O = 150:1 (v/v, 2 mL) were added to a 10 mL flask. Then the reaction mixture was stirred at 80 °C for 4 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100−200 mesh) using petroleum ether/EtOAc (10/1, v/v) as eluent to give pure **2a**. In the presence of 0.2 and 3 equiv of TEMPO, **2a** was obtained in 65% and 0% yield, respectively.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Charts for mechanistic studies as well as copies of ^{1}H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For reviews on C−C bond cleavage, see: (a) Ruhland, K. *Eur. J. Org. Chem.* **2012**, 2683. (b) Murakami, M.; Matsuda, T. *Chem. Commun.* **2011**, *47*, 1100. (c) Bonesi, S. M.; Fagnoni, M. *Chem.−Eur. J.* **2010**, *16*, 13572. (d) Winter, C.; Krause, N. *Angew. Chem.* **2009**, *121*, 6457; *Angew. Chem., Int. Ed.* **2009**, *48*, 2460. (e) Park, Y. J.; Park, J.-W.; Jun, C.-H. *Acc. Chem. Res.* **2008**, *41*, 222. (f) Seiser, T.; Cramer, N. *Org. Biomol. Chem.* **2009**, *7*, 2835. (g) Cramer, N.; Seiser, T. *Synlett* **2011**, 449. (h) Jun, C.-H. *Chem. Soc. Rev.* **2004**, *33*, 610. (i) Tobisu, M.; Chatani, N. *Chem. Soc. Rev.* **2008**, *37*, 300. (j) Crabtree, R. H. *Nature* **2000**, *408*, 415. (k) Murakami, M.; Ito, Y. In *Activation of Unreactive Bonds and Organic Synthesis*; Murai, S., Ed., Springer: Berlin, 1999; p 97. (l) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245.

(2) For some very recent examples, see: (a) Zhang, C.; Feng, P.; Jiao, N. *J. Am. Chem. Soc.* **2013**, *135*, 15257 and references cited therein. (b) Zhou, W.; Yang, Y.; Liu, Y.; Deng, G.-J. *Green Chem.* **2013**, *15*, 76. (c) Bowring, M. A.; Bergman, R. G.; Tilley, T. D. *J. Am. Chem. Soc.* **2013**, *135*, 13121. (d) Souillart, L.; Cramer, N. *Chem. Sci.* **2014**, *5*, 837. (e) Ogata, K.; Shimada, D.; Furuya, S.; Fukuzawa, S.-I. *Org. Lett.* **2013**, *15*, 1182. (f) Zhu, Y.; Yan, H.; Lu, L.; Liu, D.; Rong, G.; Mao, J. *J. Org. Chem.* **2013**, *78*, 9898. (g) Bour, J. R.; Green, J. C.; Winton, V. J.; Johnson, J. B. *J. Org. Chem.* **2013**, *78*, 1665. (h) Xu, F.; Tao, T.; Zhang, K.; Wang, X.-X.; Huang, W.; You, X.-Z. *Dalton Trans.* **2013**, *42*, 3631. (i) Ziadi, A.; Correa, A.; Martin, R. *Chem. Commun.* **2013**, *49*, 4286.

(3) For examples on C−C bond activations via strategy of oxidative addition involving transition metals, see: (a) Najera, C.; Sansano, J. M. *Angew. Chem.* **2009**, *121*, 2488; *Angew. Chem., Int. Ed.* **2009**, *48*, 2452 and references cited therein. (b) Hirata, Y.; Yada, A.; Morita, E.; Nakao, Y.; Hiyama, T.; Ohashi, M.; Ogoshi, S. *J. Am. Chem. Soc.* **2010**, *132*, 10070. (c) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (d) Murakami, M.; Tsuruta, T.; Ito, Y. *Angew. Chem.* **2000**, *112*, 2600; *Angew. Chem., Int. Ed.* **2000**, *39*, 2484. (e) Liou, S.-Y.; van der Boom, M. E.; Milstein, D. *Chem. Commun.* **1998**, 687. (f) Kondo, T.; Nakamura, A.; Okada, T.; Suzuki, N.; Wada, K.; Mitsudo, T.-A. *J. Am. Chem. Soc.* **2000**, *122*, 6319. (g) Kondo, T.; Kaneko, Y.; Taguchi, Y.; Nakamura, A.; Okada, T.; Shiotsuki, M.; Ura, Y.; Wada, K.; Mitsudo, T.-A. *J. Am. Chem. Soc.* **2002**, *124*, 6824.

(4) Reviews on *β*-carbon elimination: (a) Aïssa, C. *Synthesis* **2011**, 3389. (b) Murakami, M.; Makino, M.; Ashida, S.; Matsuda, T. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1315. (c) Satoh, T.; Miura, M. *Top. Organomet. Chem.* **2005**, *14*, 1.

(5) For selected examples, see: (a) Youn, S. W.; Kim, B. S.; Jagdale, A. R. *J. Am. Chem. Soc.* **2012**, *134*, 11308. (b) Murakami, M.; Takahashi, K.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 9307.

(6) For examples of tertiary alcohol-involved *β*-carbon elimination (also including retroallylation), see: (a) Yorimitsu, H.; Oshima, K. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 778. (b) Tarao, Y.; Wakui, H.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2001**, *123*, 10407. (c) Nishimura, T.; Araki, H.; Maeda, Y.; Uemura, S. *Org. Lett.* **2003**, *5*, 2997. (d) Terao, Y.; Wakui, H.; Nomoto, M.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2004**, *69*, 6942. (e) Terao, Y.; Wakui, H.; Nomoto, M.; Satoh, T.; Miura, M.; Nomura, M. *J. Org. Chem.* **2003**, *68*, 5236. (f) Wakui, H.; Kawasaki, S.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2004**, *126*, 8658. (g) Iwasaki, M.; Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2007**, *129*, 4463. (h) Zhao, P.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 3124. (i) Ishida, N.; Sawano, S.; Masuda, Y.; Murakami, M. *J. Am. Chem. Soc.* **2012**, *134*, 17502. (j) Waibel, M.; Cramer, N. *Angew. Chem.* **2010**, *122*, 4557; *Angew. Chem., Int. Ed.* **2010**, *49*, 4455. (k) Kondo, T.; Kodoi, K.; Nishinaga, E.; Okada, T.; Morisaki, Y.; Watanabe, Y.; Mitsudo, T.-A. *J. Am. Chem. Soc.* **1998**, *120*, 5587.

(7) For examples of secondary alcohol-involved *β*-carbon elimination, see: (a) Li, H.; Li, Y.; Zhang, X.-S.; Chen, K.; Wang, X.; Shi, Z.-J. *J. Am. Chem. Soc.* **2011**, *133*, 15244. (b) Zhang, X.-S.; Li, Y.; Li, H.; Chen, K.; Lei, Z.-Q.; Shi, Z.-J. *Chem.—Eur. J.* **2012**, *18*, 16214. (c) Chen, K.; Li, H.; Li, Y.; Zhang, X.-S.; Lei, Z.-Q.; Shi, Z.-J. *Chem. Sci.* **2012**, *3*, 1645. (d) Chen, K.; Li, H.; Lei, Z.-Q.; Li, Y.; Ye, W.-H.; Zhang, L.-S.; Sun, J.; Shi, Z.-J. *Angew. Chem.* **2012**, *124*, 9989; *Angew. Chem., Int. Ed.* **2012**, *51*, 9851. (e) Jun, C.-H.; Lee, D.-Y.; Kim, Y.-H.; Lee, H. *Organometallics* **2001**, *20*, 2928.

(8) For examples of *gem*-diol-involved *β*-carbon elimination, see: (a) Han, C.; Kim, E. H.; Colby, D. A. *J. Am. Chem. Soc.* **2011**, *133*, 5802. (b) John, J. P.; Colby, D. A. *J. Org. Chem.* **2011**, *76*, 9163. (c) Saidalimu, I.; Fang, X.; Lv, W.; Yang, X.; He, X.; Zhang, J.; Wu, F. *Adv. Synth. Catal.* **2013**, *355*, 857. (d) Prager, J. H.; Ogden, P. H. *J. Org. Chem.* **1968**, *33*, 2100.

(9) For examples of ketone-involved *β*-carbon elimination, see: (a) He, C.; Guo, S.; Huang, L.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 8273. (b) Yang, D.; Zhou, Y.; Xue, N.; Qu, J. *J. Org. Chem.* **2013**, *78*, 4171. (c) Gao, Q.; Zhu, Y.; Lian, M.; Liu, M.; Yuan, J.; Yin, G.; Wu, A. *J. Org. Chem.* **2012**, *77*, 9865. (d) Chen, Y.; Wang, Y.; Sun, Z. M.; Ma, D. *Org. Lett.* **2008**, *10*, 625. (e) Cai, S.; Wang, F.; Xi, C. *J. Org. Chem.* **2012**, *77*, 2331. (f) Malakar, C. C.; Schmidt, D.; Conrad, J.; Beifuss, U. *Org. Lett.* **2011**, *13*, 1972. (g) Kumar, P.; Zhang, K.; Louie, J. *Angew. Chem.* **2012**, *124*, 8730; *Angew. Chem., Int. Ed.* **2012**, *51*, 8602.

(10) For examples of epoxide-involved *β*-carbon elimination, see: Zhang, Y.; Wang, M.; Li, P.; Wang, L. *Org. Lett.* **2012**, *14*, 2206.

(11) For eelected examples of *N*-metal species-based *β*-carbon elimination, see: (a) Tobisu, M.; Kinuta, H.; Kita, Y.; Rémond, E.; Chatani, N. *J. Am. Chem. Soc.* **2012**, *134*, 115. (b) Nishimura, T.; Uemura, S. *J. Am. Chem. Soc.* **2000**, *122*, 12049. (c) Zhao, P.; Hartwig, J. F. *Organometallics* **2008**, *27*, 4749. (d) Zhao, P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 11618. (e) Chiba, S.; Zhang, L.; Ang, G. Y.; Hui, B. W.-Q. *Org. Lett.* **2010**, *12*, 2052.

(12) To our knowledge, there is one example of a $Ti(OPr^i)_4$-catalyzed TBHP-sourced oxygen-insertion *β*-carbon elimination, see: Basheer, A.; Mishima, M.; Marek, I. *Org. Lett.* **2011**, *13*, 4076.

(13) For examples of dioxygen-involved oxidative cleavage of C−C bonds, see: (a) Zhu, S.; Das, A.; Bui, L.; Zhou, H.; Curran, D. P.; Rueping, M. *J. Am. Chem. Soc.* **2013**, *135*, 1823. (b) Paria, S.; Halder, P.; Paine, T. K. *Angew. Chem.* **2012**, *124*, 6299; *Angew. Chem., Int. Ed.* **2012**, *51*, 6195. (c) Sun, H.; Yang, C.; Gao, F.; Li, Z.; Xia, W. *Org. Lett.* **2013**, *15*, 624. (d) Aukema, K. G.; Makris, T. M.; Stoian, S. A.; Richman, J. E.; Münck, E.; Lipscomb, J. D.; Wackett, L. P. *ACS Catal.* **2013**, *3*, 2228. (e) Hu, B.; Li, Y.; Li, Z.; Meng, X. *Org. Biomol. Chem.* **2013**, *11*, 4138. (f) Song, R.-J.; Liu, Y.; Hu, R.-X.; Liu, Y.-Y.; Wu, J.-C.; Yang, X.-H.; Li, J.-H. *Adv. Synth. Catal.* **2011**, *353*, 1467. (g) Zhang, C.; Xu, Z.; Shen, T.; Wu, G.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, *14*, 2362. (h) Paine, T. K.; England, J.; Que, L., Jr. *Chem.—Eur. J.* **2007**, *13*, 6073. (i) Liu, H.; Dong, C.; Zhang, Z.; Wu, P.; Jiang, X. *Angew. Chem.* **2012**, *124*, 12738; *Angew. Chem., Int. Ed.* **2012**, *51*, 12570.

(14) (a) Tietze, L. F., Bell, H. P., Brasche, G., Eds. *Domino Reactions in Organic Synthesis*; Wiley-VCH: Weinheim, 2006. (b) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem.* **2007**, *119*, 1590; *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (c) Nicolaou, K. C.; Montagnon, T.; Snyder, S. A. *Chem. Commun.* **2003**, 551. (d) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115.

(15) (a) Liu, Y.; Qian, J.; Lou, S.; Zhu, J.; Xu, Z. *J. Org. Chem.* **2010**, *75*, 1309. (b) Liu, Y.; Qian, J.; Lou, S.; Xu, Z. *J. Org. Chem.* **2010**, *75*, 6300. (c) Liu, Y.; Zhu, J.; Qian, J.; Jiang, B.; Xu, Z. *J. Org. Chem.* **2011**, *21*, 9096. (d) Qian, J.; Liu, Y.; Zhu, J.; Jiang, B.; Xu, Z. *Org. Lett.* **2011**, *13*, 4220. (e) Qian, J.; Liu, Y.; Cui, J.; Xu, Z. *J. Org. Chem.* **2012**, *77*, 4484. (f) Liu, Y.; Zhu, J.; Qian, J.; Xu, Z. *J. Org. Chem.* **2012**, *77*, 5411. (g) Liu, Y.; Jiang, B.; Zhang, W.; Xu, Z. *J. Org. Chem.* **2013**, *78*, 966.

(16) Zhang, W.; Zhang, J.; Liu, Y.; Xu, Z. *Synlett* **2013**, *24*, 2709.

(17) For review articles, see: (a) Herrero-Gomez, E.; Echavarren, A. M. Transition-metal-catalyzed Cycloisomerization and Nucleophilic Cycization of Enynes. In *Handbook of Cyclization Reactions*; Ma, S., Ed.; Wiley-VCH: Weinheim, 2010; Vol. 2, pp 625−686. (b) Michelet, V.; Toullec, P. Y.; Genêt, J.-P. *Angew. Chem.* **2008**, *120*, 4338; *Angew. Chem., Int. Ed.* **2008**, *47*, 4268. (c) Anorbe, L.; Dominguez, G.; Perez-Castells, J. *Chem.—Eur. J.* **2004**, *10*, 4938.

(18) For selected examples, see: (a) Wang, Z.-Q.; Wang, W.-W.; Gong, L.-B.; Tang, R.-Y.; Yang, X.-H.; Liu, Y.; Li, J.-H. *Angew. Chem.* **2011**, *123*, 9130; *Angew. Chem., Int. Ed.* **2011**, *50*, 8968. (b) Zhao, Q.; Hu, Q.; Wen, L.; Wu, M.; Hu, Y. *Adv. Synth. Catal.* **2012**, *354*, 2113. (c) Ye, S.; Gao, K.; Zhou, H.; Yang, X.; Wu, J. *Chem. Commun.* **2009**, 5406. (d) Pardo-Rodríguez, V.; Buñuel, E.; Collado-Sanz, D.; Cárdenas, D. J. *Chem. Commun.* **2012**, 10517. (e) Tsujihara, T.; Takenaka, K.; Onitsuka, K.; Hatanaka, M.; Sasai, H. *J. Am. Chem. Soc.* **2009**, *131*, 3452.

(19) Other methods for the synthesis of 3-formyl-1-indenone derivatives, see: (a) Chen, X.; Jin, J.; Wang, N.; Lu, P.; Wang, Y. *Eur. J. Org. Chem.* **2012**, 824. (b) Zhao, P.; Wang, F.; Han, K.; Li, X. *Org. Lett.* **2012**, *14*, 5506. (c) Chen, Y.; Wang, F.; Zhen, W.; Li, X. *Adv. Synth. Catal.* **2013**, *355*, 353.

(20) For synthetic usage of indenone derivatives, see: (a) Li, B.-J.; Wang, H.-Y.; Zhu, Q.-L.; Shi, Z.-J. *Angew. Chem.* **2012**, *124*, 4014; *Angew. Chem., Int. Ed.* **2012**, *51*, 3948 and references cited therein. (b) Anstead, G. M.; Ensign, J. L.; Peterson, C. S.; Katzenellenbogen, J. A. *J. Org. Chem.* **1989**, *54*, 1485. (c) Xi, Q.; Zhang, W.; Zhang, X. *Synlett* **2006**, 945. (d) Walspurger, S.; Vasilyev, A. V.; Sommer, J.; Pale, P. *Tetrahedron* **2005**, *61*, 3559.

(21) It is difficult to completely exclude H_2O in Selectfluor and CH_3CN; see: Jin, Z.; Xu, B.; Hammond, G. B. *Tetrahedron Lett.* **2011**, *52*, 1956.

(22) For examples the utilization of TEMPO as a radical scavenger, see: (a) Sibbald, P. A.; Michael, F. E. *Org. Lett.* **2009**, *11*, 1147. (b) Albéniz, A. C.; Espinet, P.; López-Fernández, R.; Sen, A. *J. Am. Chem. Soc.* **2002**, *124*, 11278.

(23) For selected examples for the redox reaction of a transition-metal complex with Selectfluor, see: (a) Wang, W.; Jasinski, J.; Hammond, G. B.; Xu, B. *Angew. Chem.* **2010**, *122*, 7405; *Angew. Chem., Int. Ed.* **2010**, *49*, 7247. (b) Xu, B.; Wang, W.; Hammond, G. B. *J. Fluorine Chem.* **2011**, *132*, 804. (c) Brenzorich, W. E., Jr.; Benitez, D.; Lackner, A. D.; Shunatona, H. P.; Tkatchouk, E.; Goddard, W. A., III; Toste, F. D. *Angew. Chem., Int. Ed.* **2010**, *122*, 5651; *Angew. Chem., Int. Ed.* **2010**, *49*, 5519. (d) Li, Z.; Song, L.; Li, C. *J. Am. Chem. Soc.* **2013**, *135*, 4640.

(24) Zhu, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 12462.

(25) Zhang, X. *J. Mol. Struct.* **2011**, *1002*, 121.

(26) Du, X.; Yang, S.; Yang, J.; Liu, Y. *Chem.—Eur. J.* **2011**, *17*, 4981.

(27) Demizu, Y.; Yamagata, N.; Nagoya, S.; Sato, Y.; Doi, M.; Tanaka, M.; Nagasawa, K.; Okuda, H.; Jurihara, M. *Tetrahedron* **2011**, *67*, 6155.