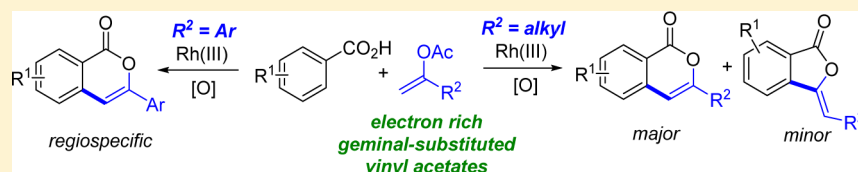


Rh(III)-Catalyzed Oxidative Coupling of Benzoic Acids with Geminal-Substituted Vinyl Acetates: Synthesis of 3-Substituted Isocoumarins

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Supporting Information

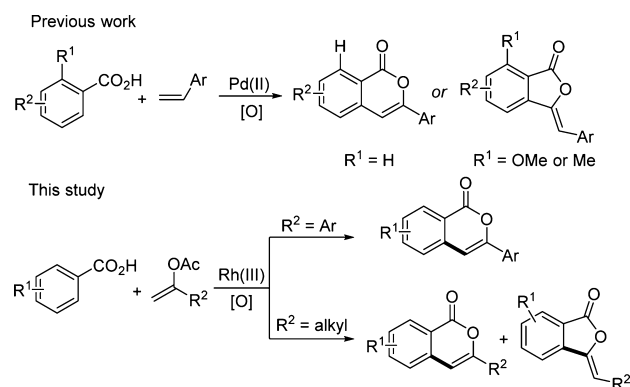


ABSTRACT: The Rh(III)-catalyzed C–H activation initiated cyclization of benzoic acids with electron-rich geminal-substituted vinyl acetates was described. The reaction was employed to prepare a range of 3-aryl and 3-alkyl substituted isocoumarins selectively.

Isocoumarins, especially 3-substituted isocoumarins that have no substituents at the 4-position, are an important class of biologically active scaffolds and present in a large number of pharmaceuticals and natural products.^{1,2} Plenty of methods have been developed for the formation of isocoumarin skeletons,^{3,4} mainly including the annulation of internal alkynes by halogen- or triflate-containing aromatic esters,^{4a,b} the electrophilic cyclization of 2-(alkynyl)benzoic acid derivatives,^{4c–e} and the coupling of 2-halo benzoic acid derivatives with terminal alkynes, followed by subsequent cyclization.^{4f,g} Recently, several novel routes for the construction of 3-substituted isocoumarins were developed involving the copper-catalyzed sequential cyclization of 2-halobenzoic acids or their derivatives with 1,3-diketones.^{4h–k} In addition, Ji et al. disclosed that, starting from 1-(2-halophenyl)-3-phenylpropane-1,3-diones, 3-substituted isocoumarins could be formed through a copper-catalyzed cascade intramolecular Ullmann-type coupling-rearrangement process.^{4l} However, most of these strategies were limited by the use of halogenated aromatic carboxylic acid derivatives as substrates.

Recently, direct C–H bond functionalization as an atom- and step-economical process has become a powerful protocol in organic synthesis.⁵ In this context, the C–H activation/annulation strategies were applied for the construction of benzo-fused heterocycles including isocoumarins.⁶ In 2007, Satoh and Miura et al. disclosed a Rh/Cu-catalyzed oxidative annulation reaction of internal alkynes by benzoic acids for the synthesis of 3,4-disubstituted isocoumarins.^{7a,b} Later, Ackermann et al. reported a similar transformation catalyzed by a ruthenium complex.^{7c,d} Recently, Miura and Lee et al., respectively, discovered that the palladium-catalyzed direct oxidative coupling of benzoic acids with vinylarenes could afford 3-substituted isocoumarins or 3-benzylidenephthalides (Scheme 1).⁸ Lee and his co-workers also found that the substituents on the benzoic acids have a significant effect on the reaction selectivity (Scheme 1). When *ortho*-substituted

Scheme 1. Synthesis of 3-Substituted Isocoumarins Based on C–H Functionalization



benzoic acids were treated with vinylarenes, the corresponding 3-benzylidenephthalides were formed selectively, which signified that 7-substituted isocoumarins could not be synthesized using this methodology. Furthermore, other than reactive acrylates^{8a} and vinylarenes, electron-rich alkenes, such as vinyl esters and vinyl ethers, were not involved in the transformation.⁸ Herein, we report a novel approach to prepare 3-aryl- and 3-alkyl-substituted isocoumarins selectively based on the Rh(III)-catalyzed oxidative coupling between benzoic acid and electron-rich geminal-substituted vinyl acetates (Scheme 1).

The transition-metal-catalyzed oxidative C–H olefination with electron-deficient and electron-neutral alkenes has been extensively studied.⁹ However, there are only a few reports on the oxidative C–H alkenylation with electron-rich alkenes.^{10,11} Considering its usability and accessibility, it is of interest to

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Table 1. Reaction Optimization^a

entry	cat.	oxidant	additive	solvent	yield (%) ^b
1	[RhCp*Cl ₂] ₂	Cu(OAc) ₂ ·H ₂ O		PhMe	21
2	[RhCp*Cl ₂] ₂	CuO		PhMe	39
3	[RhCp*Cl ₂] ₂	CuO		<i>t</i> -Am-OH	32
4 ^c	[RhCp*Cl ₂] ₂	CuO		PhMe/ <i>t</i> -Am-OH (2:1)	31
5	[RhCp*Cl ₂] ₂	CuO	KOAc	PhMe/ <i>t</i> -Am-OH	65
6	[RhCp*Cl ₂] ₂	CuO	KOAc/KI	PhMe/ <i>t</i> -Am-OH	50
7	[RhCp*Cl ₂] ₂	CuO	KOAc/LiCl	PhMe/ <i>t</i> -Am-OH	46
8 ^d	[RhCp*Cl ₂] ₂	CuO	KOAc/LiCl/KI	PhMe/ <i>t</i> -Am-OH	75
9		CuO	KOAc/LiCl/KI	PhMe/ <i>t</i> -Am-OH	0
10	[RhCp*Cl ₂] ₂		KOAc/LiCl/KI	PhMe/ <i>t</i> -Am-OH	0

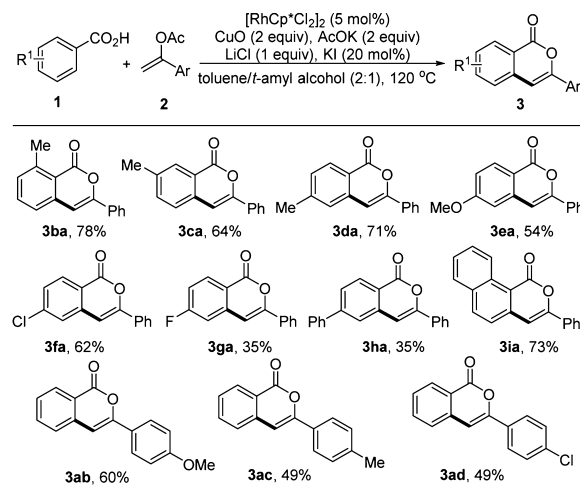
^aReaction conditions: **1a** (0.8 mmol), **2a** (2.0 mmol), [RhCp*Cl₂]₂ (0.04 mmol), oxidant (1.6 mmol), additive, solvent (2 or 3 mL), 120 °C.

^bIsolated yield of **3aa**. ^c*tert*-Amyl alcohol (1 mL). ^dKOAc (1.6 mmol), LiCl (0.8 mmol), KI (0.16 mmol).

investigate the direct olefination on aromatic rings with vinyl acetate derivatives.^{12,13} Our initial study focused on the reaction between benzoic acid (**1a**) and 1-phenylvinyl acetate (**2a**). To our delight, when **1a** was treated with **2a** in the presence of 5 mol % of [RhCp*Cl₂]₂ and 2 equiv of Cu(OAc)₂·H₂O in toluene at 120 °C, 3-phenylisochromen-1-one (**3aa**) was formed in 21% yield after 48 h (Table 1, entry 1). When Cu(OAc)₂·H₂O was replaced by CuO, the yield of **3aa** was increased to 39% (Table 1, entry 2). Several solvents were tested, and the reactions performed in *tert*-amyl alcohol or toluene/*tert*-amyl alcohol (2:1) gave slightly lower yields (32% and 31%, respectively; Table 1, entries 3 and 4).¹⁴ Interestingly, the addition of KOAc increased the yield of **3aa** up to 65% (Table 1, entry 5).¹⁵ Subsequently, screening of a range of additives suggested that the addition of both KI and LiCl was also effective for the cyclization (Table 1, entries 6–8).¹⁶ The desired product was formed in 75% yield in the presence of KOAc as base and LiCl/KI as additives (Table 1, entry 8). In addition, treatment of benzoic acid (**1a**) with 1-phenylvinyl acetate (**2a**) in the absence of either [RhCp*Cl₂]₂ or CuO did not afford the desired product (entries 9 and 10).

With the optimized conditions in hand, the scope of the benzoic acids and 1-arylviny acetates was examined (Table 2). The reactions of all the 2-, 3-, and 4-methylbenzoic acids with **2a** led to the formation of the corresponding isocoumarins in high yields (**3ba**–**3da**). It is noteworthy that the regioselectivity of the transformations was not affected by the substituents on the benzoic acids, which is different from Lee's work.^{8b} Moreover, both electron-rich and electron-deficient benzoic acids were compatible substrates, and moderate to good yields of products (**3ea**–**3ha**) were obtained. When 1-naphthoic acid (**1i**) was treated with **2a**, the corresponding cyclization product **3ia** could be obtained in 73% yield. In addition, several substituted 1-phenylvinyl acetates also reacted with benzoic acid (**1a**) smoothly and gave the corresponding products in moderate yields (**3ab**–**3ad**).

Subsequently, we were delighted to find that 1-alkylvinyl acetates could also react with benzoic acids under the current conditions (Table 3).¹⁷ The cyclization of a range of benzoic acids with isopropenyl acetate produced the corresponding 3-methyl isocoumarins **3ae**–**3he**, accompanied by minor amounts of 3-ethylidenisobenzofuranones **4ae**–**4ie** (entries

Table 2. Cyclization of Arylcarboxylic Acids with 1-Arylviny Acetates^a

^aReaction conditions: **1** (0.8 mmol), **2** (2.0 mmol), [RhCp*Cl₂]₂ (0.04 mmol), CuO (1.6 mmol), KOAc (1.6 mmol), LiCl (0.8 mmol), KI (0.16 mmol), PhMe/*t*-Am-OH (2:1) (3 mL), 120 °C.

1–9).¹⁸ The reactions of 1- and 2-naphthoic acids with isopropenyl acetate also took place smoothly (entry 10 and 11). Notably, starting from 2-naphthoic acids, **3ke** and **4ke** derived from the C–H activation at the C-3 rather than the C-1 position was selectively formed perhaps due to the steric hindrance. Other 1-alkylvinyl acetates, such as hex-1-en-2-yl acetate (**2f**), 4-phenylbut-1-en-2-yl acetate (**2g**), and methyl 2-acetoxyacrylate (**2h**), were also tested, and only the corresponding 3-alkyl isocoumarins **3af**–**3ah** were isolated in low yields (entries 12–14). Notably, the cheap and simple vinyl acetate (**2h**) could also react with benzoic acid (**1a**) under the standard conditions. However, the corresponding isocoumarin **3ai** was produced in only 14% yield (entry 13).¹¹ Furthermore, cyclohexenyl acetate and 1-propenyl acetate were not suitable substrates for this transformation.

To figure out the mechanism, several experiments were conducted. First, treatment of prop-1-en-2-yl benzoate (**5**) under standard conditions gave only a trace amount of isocoumarin product **3aa** (see the Supporting Information),

Table 3. Cyclization of Arylcarboxylic Acids with 2-Alkylvinyl Acetates^{a,b,c}

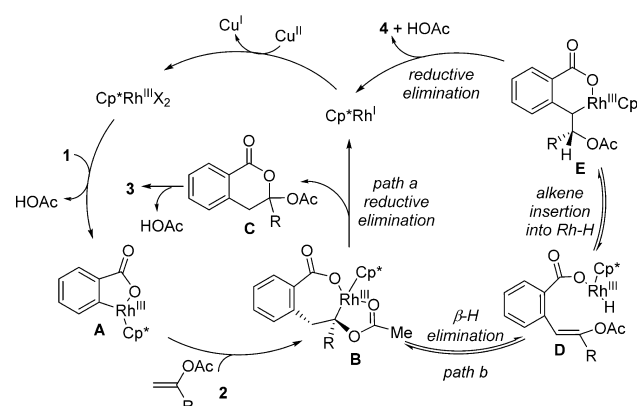
entry	benzoic acids	R ²	product	yield/% (3:4) ^b	entry	benzoic acids	R ²	product	yield/% (3:4) ^b
1		Me		88 (2:1)	8		Me		66 (4.5:1)
2		Me		93 (2.7:1)	9		Me		28 (3.7:1)
3		Me		90 (2.6:1)	10		Me		87 (3.6:1)
4		Me		85 (2.9:1)	11		Me		85 (2.5:1)
5		Me		88 (2.3:1)	12 ^c		Bu		20
6		Me		82 (3.1:1)	13		2-phenylethyl		42
7		Me		88 (3.6:1)	14		CO ₂ Me		43
					15		H		14

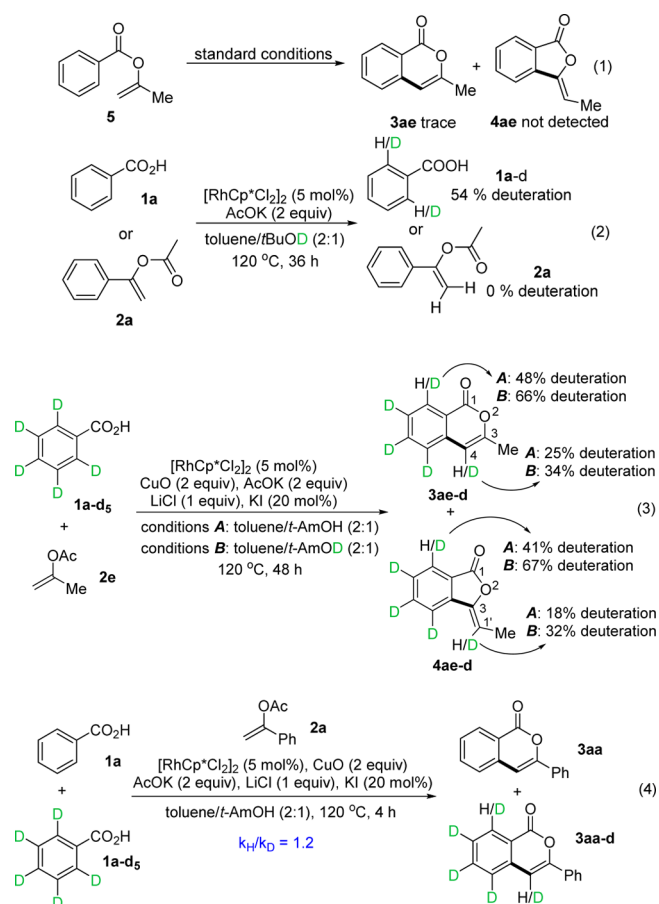
^aReaction conditions: **1** (0.8 mmol), **2** (2.0 mmol), [RhCp*Cl₂]₂ (0.04 mmol), CuO (1.6 mmol), KOAc (1.6 mmol), LiCl (0.8 mmol), KI (0.16 mmol), PhMe/*t*-Am-OH (2:1) (3 mL), 120 °C. ^bIsolated yield. ^cTrace amount of **4af** was also observed by in situ ¹H NMR.

indicating that the transvinylolation between **1a** and **2a** might not be involved in the reaction process (eq 1).^{19,20} Deuterium labeling experiments of benzoic acid (**1a**) and 1-phenylvinyl acetate (**2a**) were carried out, respectively, under the same reaction conditions (eq 2). Only benzoic acid **1a** was deuterated, indicating the possibility of *ortho*-C–H olefination of benzoic acid with 1-phenylvinyl acetate.⁹ Notably, no 4-substituted isocoumarins were observed in all examples shown in Tables 2 and 3, which suggested the highly regioselective insertion of alkenes to arylrhodium intermediates. The formation of 3-ethylidenisobenzofuranones **4** was also consistent with this regiochemistry. Furthermore, the reaction of *d*₅-benzoic acid **1a-d**₅ with isopropenyl acetate (**2e**) was conducted under standard conditions (eq 3). The incorporation of deuterium at the C-4 position of **3ae-d** (25% and 34%) and the C-1' position of **4ae-d** (18% and 32%) was confirmed by ¹H NMR (see the Supporting Information). Moreover, the competing reactions of **1a** and **1a-d**₅ with 1-phenylvinyl acetate (**2a**) were conducted in the same flask (eq 4). The KIE value (*k*_H/*k*_D = 1.2) was calculated based on the ratio of products **3aa** and **3aa-d**, which suggested that the cleavage of the C–H bond maybe not involved in the rate-limiting step.

On the basis of these experiments, a plausible mechanism was proposed (Scheme 2). First, a rhodacycle **A** is formed through the coordination of the carboxylate oxygen of **1** to the Cp*Rh(III) center, followed by *ortho*-rhodation.^{9a–d} Subsequently, regioselective insertion of geminal-substituted vinyl acetate **2** into the Rh–C bond leads to the formation of rhodacycle **B**. The phenyl migration from the Rh center to the

Scheme 2. Proposed Catalytic Cycle





C-2 position of **2** is favored, perhaps due to the coordination between the acetoxy group and the Rh center, which was also proposed by Mardsen and co-workers.¹¹ When R is an aryl group, the corresponding rhodacycle **B** prefers to undergo reductive elimination to give intermediate **C** and Cp*Rh(I) (path a, in Scheme 2). The resulting Cp*Rh(I) is oxidized by Cu(II) to regenerate Cp*Rh(III). Elimination of acetic acid from **C** affords the final product **3**. This pathway may explain the regiospecific formation of isocoumarin product **3** starting from 1-arylviny acetates. When R is the methyl group, besides path a, the corresponding rhodacycle **B** may also undergo reversible β -hydride elimination to afford rhodium hydride intermediate **D** (path b, in Scheme 2). Intramolecular alkene insertion to the Rh–H bond led to the formation of two regioisomeric rhodacycles **B** or **E**. Reductive elimination of intermediate **E**, followed by elimination of acetic acid, produced another isomeric product **4**. The H/D exchange of rhodium hydride intermediate **D** in the presence of *t*-AmOD or in situ formed DOAc may cause the final introduction of deuterium at the C-4 position of **3** and the C-1' position of **4** selectively (eq 3).²¹ Moreover, the reaction between *d*₅-benzoic acid **1a-d**₅ and 1-phenylvinyl acetate (**2a**) was also conducted under standard conditions, and almost no deuterium was incorporated at the C-4 position of **3aa-d** (see the Supporting Information), which is consistent with the proposed catalytic cycle.

In conclusion, we have developed a Rh(III)-catalyzed protocol for the synthesis of 3-substituted isocoumarins by a C–H activation/annulation reaction of electron-rich geminal-substituted vinyl acetates. The reactions starting from 1-aryl vinyl acetates afford the corresponding 3-aryl substituted isocoumarins regiospecifically. However, the reactions of 1-

alkyl vinyl acetates with benzoic acids lead to the formation of 3-alkyl substituted isocoumarins as major products. This protocol constitutes an efficient and versatile pathway to a range of isocoumarin derivatives.

EXPERIMENTAL SECTION

General Information. All commercial reagents were used without further purification. ¹H and ¹³C NMR spectra were recorded at 400 or 500 MHz in CDCl₃ as solvent. High-resolution mass spectra were recorded on an FT-MS instrument using the ESI technique. IR spectra were recorded on an FT-IR spectrophotometer, with absorptions reported in wavenumbers (cm^{−1}).

General Procedures for Cyclizations of Benzoic Acids with Geminal-Substituted Vinyl Acetates. To a 25 mL tube, benzoic acid **1** (0.8 mmol, 1 equiv), [RhCp*Cl₂]₂ (0.04 mmol, 5 mol %), CuO (1.6 mmol, 2 equiv), AcOK (1.6 mmol, 2 equiv), LiCl (0.8 mmol, 1 equiv), KI (0.16 mmol, 0.2 equiv), geminal-substituted vinyl acetate **2** (2 mmol, 2.5 equiv), 1 mL of *tert*-amyl alcohol, and 2 mL of toluene were added. Then, the tube was sealed with a Teflon lined cap, and the reaction mixture was stirred at 120 °C for 48 h. Subsequently, the reaction mixture was concentrated under vacuum. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 40:1–20:1) to afford the product.

3-Phenyl-1H-isochromen-1-one (3aa).^{22a} Light yellow solid, mp 88–89 °C, isolated yield 75% (133 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.31–8.27 (m, 1H), 7.89–7.83 (m, 2H), 7.72–7.67 (m, 1H), 7.50–7.41 (m, 5H), 6.92 (s, 1H); ¹³C NMR (400 MHz, CDCl₃) δ 162.2, 153.5, 137.4, 134.8, 131.9, 129.9, 129.5, 128.8, 128.1, 126.0, 125.2, 120.4, 101.8; IR (KBr, cm^{−1}) 3060, 2979, 2919, 1727, 1635, 1483, 1232, 1064, 1027, 765, 688.

8-Methyl-3-phenyl-1H-isochromen-1-one (3ba).^{22b} Light yellow solid; mp 133–135 °C, yield: 78% (147 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.88–7.83 (m, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47–7.39 (m, 3H), 7.29 (d, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 6.85 (s, 1H), 2.85 (s, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 161.5, 153.0, 143.4, 139.0, 133.9, 131.9, 131.0, 129.7, 128.7, 125.1, 124.2, 118.9, 102.2, 23.1; IR (KBr, cm^{−1}) 3099, 3079, 3060, 3027, 2968, 2925, 1720, 1643, 1448, 1074, 1051, 858, 781, 759, 690.

7-Methyl-3-phenyl-1H-isochromen-1-one (3ca).^{22c} Light yellow solid; mp 138–139 °C, yield: 64% (121 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.12 (s, 1H), 7.88 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.53 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.49–7.38 (m, 5H), 6.92 (s, 1H), 2.48 (s, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 162.4, 152.8, 138.4, 136.1, 135.0, 132.1, 129.7, 129.3, 128.7, 125.9, 125.1, 120.4, 101.7, 21.3; IR (KBr, cm^{−1}) 3087, 3052, 3035, 2921, 2856, 1724, 1639, 1498, 1137, 1066, 852, 784, 763, 696, 534.

6-Methyl-3-phenyl-1H-isochromen-1-one (3da).^{22c} White solid; mp 110–113 °C, yield: 71% (134 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.19 (d, *J* = 8.1 Hz, 1H), 7.90–7.86 (m, 2H), 7.49–7.41 (m, 3H), 7.33–7.29 (m, 1H), 7.28 (s, 1H), 6.89 (s, 1H), 2.49 (s, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 162.3, 153.6, 145.9, 137.6, 132.1, 129.8, 129.6, 129.5, 128.7, 125.9, 125.2, 118.1, 101.7, 21.9; IR (KBr, cm^{−1}) 3103, 3085, 3054, 3033, 2915, 2852, 1714, 1614, 1450, 1064, 896, 771, 757, 682.

6-Methoxy-3-phenyl-1H-isochromen-1-one (3ea).^{22c} White solid; mp 143–144 °C, yield: 54% (109 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.22 (d, *J* = 8.8 Hz, 1H), 7.90–7.85 (m, 2H), 7.49–7.41 (m, 3H), 7.03 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.88 (s, 1H), 6.87 (d, *J* = 2.5 Hz, 1H), 3.93 (s, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 164.7, 162.0, 154.1, 139.8, 132.0, 131.8, 129.9, 128.7, 125.2, 116.5, 113.7, 107.9, 101.8, 55.6; IR (KBr, cm^{−1}) 3081, 3035, 2971, 2944, 2840, 1708, 1604, 1452, 1263, 1064, 862, 761, 688.

6-Chloro-3-phenyl-1H-isochromen-1-one (3fa).^{22d} Light yellow solid; mp 199–203 °C, yield: 62% (127 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.26 (d, *J* = 8.5 Hz, 1H), 7.92–7.87 (m, 2H), 7.53–7.45 (m, 5H), 6.90 (s, 1H); ¹³C NMR (500 MHz, CDCl₃) δ 161.4, 155.0, 141.5, 138.9, 131.6, 131.3, 130.4, 128.9, 128.5, 125.4, 118.8, 100.7; IR (KBr, cm^{−1}) 3101, 3066, 2921, 2850, 1712, 1633, 1450, 1322, 1236, 1060, 891, 769, 754, 678, 642.

6-Fluoro-3-phenyl-1H-isochromen-1-one (3ga):^{22a} Light yellow solid; mp 163–165 °C, yield: 35% (67 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.36 (dd, *J* = 8.6, 5.6 Hz, 1H), 7.95–7.85 (m, 2H), 7.55–7.45 (m, 3H), 7.24–7.15 (m, 2H), 6.93 (s, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 168.0, 165.4, 161.3, 154.9, 140.2, 140.1, 133.0, 132.9, 131.5, 130.3, 128.9, 125.4, 117.0, 116.9, 116.5, 116.3, 111.6, 111.4, 101.2, 101.2; IR (KBr, cm⁻¹) 3103, 3087, 3072, 3037, 2921, 2852, 1714, 1569, 1454, 1349, 1257, 1066, 883, 771, 682.

3,6-Diphenyl-1H-isochromen-1-one (3ha): Light yellow solid; mp 170–173 °C, yield: 35% (84 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.39 (d, *J* = 8.2 Hz, 1H), 7.97–7.90 (m, 2H), 7.74 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.72–7.67 (m, 3H), 7.56–7.44 (m, 7H), 7.03 (s, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 162.9, 154.7, 148.4, 140.1, 138.7, 132.7, 130.9, 130.7, 129.7, 129.5, 129.4, 128.1, 127.9, 126.0, 124.8, 119.9, 102.6; IR (KBr, cm⁻¹) 3095, 2919, 2852, 1712, 1608, 1446, 1342, 1068, 892, 756, 690; HRMS (ESI) *m/z*: calcd. for C₂₁H₁₄NaO₂ [M + Na]⁺ 321.0892, found 321.0894.

3-Phenyl-1H-benzo[h]isochromen-1-one (3ia): Light yellow solid; mp 185–188 °C, yield: 73% (159 mg); ¹H NMR (500 MHz, CDCl₃) δ 9.75 (d, *J* = 8.7 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 8.00–7.94 (m, 2H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.78 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.63 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.54–7.45 (m, 4H), 7.06 (s, 1H); ¹³C NMR (500 MHz, CDCl₃): δ 161.4, 155.0, 140.1, 136.3, 132.9, 131.7, 131.6, 130.2, 129.4, 128.8, 128.6, 126.6, 125.4, 123.9, 113.8, 102.6; IR (KBr, cm⁻¹) 3097, 3054, 2962, 2925, 2852, 1708, 1639, 1598, 1047, 1031, 852, 740, 682; HRMS (ESI) *m/z*: calcd. for C₁₉H₁₂NaO₂ [M + Na]⁺ 295.0735, found 295.0731.

3-(4-Methoxyphenyl)-1H-isochromen-1-one (3ab):^{22a} Light yellow solid; mp 118–123 °C, yield: 60% (121 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.28 (d, *J* = 8.2 Hz, 1H), 7.84–7.78 (m, 2H), 7.68 (td, *J* = 7.8, 1.3 Hz, 1H), 7.45 (ddd, *J* = 4.7, 3.7, 1.9 Hz, 2H), 6.98–6.95 (m, 2H), 6.81 (s, 1H), 3.86 (s, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 162.4, 161.0, 153.7, 137.9, 134.7, 129.5, 127.6, 126.7, 125.6, 124.5, 120.1, 114.2, 100.2, 55.3; IR (KBr, cm⁻¹) 3076, 2996, 2960, 2931, 2836, 1727, 1633, 1600, 1511, 1255, 1234, 1178, 1064, 1027, 823, 754, 686.

3-(*p*-Tolyl)-1H-isochromen-1-one (3ac):^{22a} Light yellow solid; mp 117–119 °C, yield: 49% (93 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.28 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.78–7.73 (m, 2H), 7.72–7.66 (m, 1H), 7.48–7.43 (m, 2H), 7.25 (dd, *J* = 8.5, 0.6 Hz, 2H), 6.88 (s, 1H), 2.39 (s, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 162.3, 153.7, 140.2, 137.6, 134.8, 129.5, 129.5, 129.1, 127.8, 125.8, 125.1, 120.3, 101.0, 21.3; IR (KBr, cm⁻¹) 3066, 3031, 2952, 2919, 2854, 1731, 1629, 1064, 815, 752, 686, 526.

3-(4-Chlorophenyl)-1H-isochromen-1-one (3ad):^{22a} Light yellow solid; mp 148–150 °C, yield: 49% (101 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.31–8.27 (m, 1H), 7.82–7.78 (m, 2H), 7.75–7.70 (m, 1H), 7.50 (ddd, *J* = 7.8, 5.4, 1.7 Hz, 2H), 7.45–7.40 (m, 2H), 6.92 (s, 1H); ¹³C NMR (400 MHz, CDCl₃): δ 161.9, 152.4, 137.2, 135.9, 134.9, 130.4, 129.6, 129.0, 128.3, 126.4, 126.0, 120.5, 102.0; IR (KBr, cm⁻¹) 3097, 3035, 2962, 2921, 1722, 1639, 1492, 1068, 1012, 823, 750, 682, 524.

3-Methyl-1H-isochromen-1-one (3ae):^{23a} White solid, mp 75–77 °C, yield 59% (76 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.22 (d, *J* = 8.5 Hz, 1H), 7.65 (ddd, *J* = 8.6, 7.6, 1.3 Hz, 1H), 7.45–7.40 (m, 1H), 7.32 (d, *J* = 7.9 Hz, 1H), 6.24 (s, 1H), 2.26 (s, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 162.9, 154.5, 137.6, 134.7, 129.4, 127.5, 124.8, 119.8, 103.5, 19.5; IR (KBr, cm⁻¹) 3076, 3029, 2950, 2919, 1720, 1660, 1162, 1068, 757, 688.

3,8-Dimethyl-1H-isochromen-1-one (3be): Light yellow solid; mp 91–93 °C, yield: 68% (95 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.47 (t, *J* = 7.7 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.8 Hz, 1H), 6.16 (d, *J* = 0.9 Hz, 1H), 2.79 (s, 3H), 2.22 (d, *J* = 1.0 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 162.2, 154.0, 143.2, 139.1, 133.8, 130.3, 123.0, 118.3, 103.9, 23.1, 19.3; IR (KBr, cm⁻¹) 3091, 3068, 3043, 2969, 2921, 2848, 1724, 1668, 1573, 1475, 1390, 1193, 1162, 1037, 987, 835, 800, 779, 688; HRMS (ESI) *m/z*: calcd. for C₁₁H₁₀NaO₂ [M + Na]⁺ 197.0579, found 197.0574.

3,7-Dimethyl-1H-isochromen-1-one (3ce):^{23b} White solid, mp 123–126 °C, yield 65% (91 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.04

(d, *J* = 0.8 Hz, 1H), 7.48 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 6.22 (s, 1H), 2.44 (s, 3H), 2.26 (s, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 163.1, 153.6, 137.6, 135.9, 135.1, 129.1, 124.7, 119.7, 103.3, 21.2, 19.5; IR (KBr, cm⁻¹) 3064, 3031, 2958, 2921, 1729, 1660, 1344, 1153, 1066, 979, 844, 738, 694.

3,6-Dimethyl-1H-isochromen-1-one (3de):^{23c} Light yellow solid, mp 70–72 °C, yield 63% (88 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, *J* = 8.1 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.10 (s, 1H), 6.17 (s, 1H), 2.44 (s, 3H), 2.25 (s, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 163.0, 154.5, 145.7, 137.7, 129.3, 128.8, 124.8, 117.4, 103.4, 21.9, 19.6; IR (KBr, cm⁻¹) 3079, 2958, 2919, 1718, 1660, 1160, 1056, 775, 686.

6-Methoxy-3-methyl-1H-isochromen-1-one (3ee):^{23a} White solid, mp 100–103 °C, yield 61% (93 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.14 (d, *J* = 8.8 Hz, 1H), 6.97 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.70 (d, *J* = 2.5 Hz, 1H), 6.17 (s, 1H), 3.89 (s, 3H), 2.25 (d, *J* = 0.9 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 164.6, 162.7, 155.1, 140.0, 131.6, 115.8, 113.0, 106.9, 103.5, 55.5, 19.6; IR (KBr, cm⁻¹) 3074, 3014, 2921, 2842, 1716, 1658, 1602, 1357, 1253, 1222, 1056, 999, 858, 777, 686.

6-Chloro-3-methyl-1H-isochromen-1-one (3fe):^{23b} White solid, mp 148–150 °C, yield 62% (97 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.16 (d, *J* = 8.5 Hz, 1H), 7.39 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.31 (d, *J* = 2.0 Hz, 1H), 6.19 (s, 1H), 2.29 (d, *J* = 0.9 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 162.0, 156.0, 141.3, 138.9, 131.1, 128.0, 124.3, 118.2, 102.6, 19.7; IR (KBr, cm⁻¹) 3089, 3064, 3041, 2966, 2927, 1747, 1654, 1598, 1558, 1336, 1159, 1054, 864, 840, 775, 680.

6-Fluoro-3-methyl-1H-isochromen-1-one (3ge):^{23b} Light yellow solid, mp 88–89 °C, yield 69% (98 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.22 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.10 (td, *J* = 8.6, 2.5 Hz, 1H), 6.95 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.20 (s, 1H), 2.26 (d, *J* = 0.9 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 167.9, 165.3, 161.8, 156.0, 140.3, 140.2, 132.8, 132.7, 116.3, 116.3, 115.8, 115.6, 110.5, 110.3, 103.0, 103.0, 19.6; IR (KBr, cm⁻¹) 3074, 2975, 2923, 1731, 1662, 1618, 1344, 1168, 1058, 771, 678.

3-Methyl-6-phenyl-1H-isochromen-1-one (3he): White solid; mp 142–144 °C, yield: 54% (102 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.31 (d, *J* = 8.3 Hz, 1H), 7.70–7.63 (m, 3H), 7.54–7.48 (m, 3H), 7.44 (ddd, *J* = 5.8, 4.4, 2.0 Hz, 1H), 6.31 (s, 1H), 2.31 (d, *J* = 0.9 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 162.8, 154.9, 147.5, 139.5, 138.1, 130.0, 129.0, 128.6, 127.3, 126.6, 123.0, 118.6, 103.6, 19.6; IR (KBr, cm⁻¹) 3066, 3033, 2958, 2921, 2848, 1720, 1658, 1560, 1160, 1066, 889, 765, 690; HRMS (ESI) *m/z*: calcd. for C₁₆H₁₂NaO₂ [M + Na]⁺ 259.0735, found 259.0729.

Methyl 3-Methyl-1-oxo-1H-isochromene-6-carboxylate (3ie): Light yellow solid; mp 178–181 °C, yield: 22% (38 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.29 (d, *J* = 8.2 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 8.00 (s, 1H), 6.31 (s, 1H), 3.97 (s, 3H), 2.30 (s, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 165.8, 162.1, 155.4, 137.5, 135.5, 129.7, 127.7, 126.4, 122.8, 103.3, 52.6, 19.6; IR (KBr, cm⁻¹) 3072, 3010, 2960, 2921, 2848, 1737, 1718, 1666, 1338, 1290, 1105, 964, 914, 844, 744, 680; HRMS (ESI) *m/z*: calcd. for C₁₂H₁₀NaO₄ [M + Na]⁺ 241.0477, found 241.0473.

3-Methyl-1H-benzo[h]isochromen-1-one (3je):^{23d} Light yellow solid; mp 152–154 °C, yield: 68% (114 mg); ¹H NMR (500 MHz, CDCl₃) δ 9.64 (d, *J* = 8.6 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.69 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.54 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 1H), 6.24 (s, 1H), 2.27 (d, *J* = 0.9 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 162.1, 156.3, 140.2, 136.1, 132.5, 131.4, 129.1, 128.5, 126.4, 126.3, 123.1, 112.8, 104.6, 19.5; IR (KBr, cm⁻¹) 3110, 3076, 3014, 2923, 1716, 1589, 1249, 1051, 840, 790, 756, 690; HRMS (ESI) *m/z*: calcd. for C₁₄H₁₀NaO₂ [M + Na]⁺ 233.0578, found 233.0576.

3-Methyl-1H-benzoglischromen-1-one (3ke):^{23e} Light yellow solid; mp 194–197 °C, yield: 61% (103 mg); ¹H NMR (400 MHz, CDCl₃) δ 8.84 (s, 1H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.69 (s, 1H), 7.60 (ddd, *J* = 8.3, 6.8, 1.2 Hz, 1H), 7.50 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 6.31 (s, 1H), 2.28 (d, *J* = 0.8 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 163.0, 152.7, 136.5, 132.3, 132.0, 131.7, 129.6, 129.2, 127.5, 126.2, 122.7, 118.5, 103.3, 19.6; IR (KBr, cm⁻¹)

3050, 2956, 2919, 1731, 1666, 1384, 1243, 1157, 1126, 1060, 898, 784, 754, 478.

3-Butyl-1H-isochromen-1-one (3af):^{23f} Light yellow oil; yield: 20% (32 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.68 (td, *J* = 7.8, 1.3 Hz, 1H), 7.48–7.43 (m, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 6.27 (s, 1H), 2.57–2.52 (m, 2H), 1.71 (dt, *J* = 15.2, 7.5 Hz, 2H), 1.47–1.38 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 163.1, 158.3, 137.6, 134.6, 129.4, 127.5, 124.9, 120.1, 102.8, 33.2, 28.9, 22.1, 13.7; IR (KBr, cm⁻¹) 3070, 2958, 2929, 2871, 1727, 1656, 1483, 1160, 1103, 1054, 1022, 756, 690.

3-Phenethyl-1H-isochromen-1-one (3ag):^{23g} Light yellow oil; yield: 42% (84 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.31–8.27 (m, 1H), 7.69 (td, *J* = 7.6, 1.3 Hz, 1H), 7.50–7.46 (m, 1H), 7.32 (ddd, *J* = 8.3, 7.5, 5.3 Hz, 3H), 7.23 (dd, *J* = 10.3, 4.3 Hz, 3H), 6.24 (s, 1H), 3.09–3.03 (m, 2H), 2.89–2.84 (m, 2H); ¹³C NMR (500 MHz, CDCl₃): δ 163.0, 156.9, 140.3, 137.4, 134.7, 129.5, 128.5, 128.3, 127.7, 126.3, 125.1, 120.1, 103.5, 35.4, 33.2; IR (KBr, cm⁻¹) 3060, 3025, 2923, 2856, 1726, 1656, 1483, 1159, 1052, 1024, 970, 754, 688.

Methyl 1-Oxo-1H-isochromene-3-carboxylate (3ah):²⁴ Light yellow solid; mp 167–170 °C, yield: 43% (70 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.38 (d, *J* = 7.8 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.52 (s, 1H), 3.99 (s, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 160.7, 160.6, 143.2, 135.1, 134.9, 130.8, 130.0, 127.6, 122.7, 112.3, 52.9; IR (KBr, cm⁻¹) 3081, 3045, 3012, 2956, 2917, 2848, 1726, 1716, 1321, 1097, 1052, 1024, 767.

1H-Isichromen-1-one (3ai):²⁵ Light yellow liquid, yield 14% (16 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.31–8.24 (m, 1H), 7.71 (td, *J* = 7.7, 1.3 Hz, 1H), 7.53–7.48 (m, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.27 (d, *J* = 5.6 Hz, 1H), 6.50 (d, *J* = 5.6 Hz, 1H); ¹³C NMR (500 MHz, CDCl₃) δ 162.1, 144.6, 136.4, 134.7, 129.5, 128.5, 125.5, 121.8, 106.9; IR (KBr, cm⁻¹) 3106, 3085, 3014, 2966, 2925, 1721, 1635, 1486, 1249, 1051, 1002, 790, 690.

(Z)-3-Ethylideneisobenzofuran-1(3H)-one (4ae):^{26a} Light yellow liquid, yield 29% (37 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.89 (dt, *J* = 7.7, 0.9 Hz, 1H), 7.68 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 7.64 (dt, *J* = 7.8, 1.0 Hz, 1H), 7.54–7.49 (m, 1H), 5.69 (q, *J* = 7.3 Hz, 1H), 2.04 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 167.1, 146.3, 139.5, 134.2, 129.3, 125.2, 124.4, 119.5, 104.1, 11.2; IR (KBr, cm⁻¹) 3052, 2917, 2858, 1776, 1693, 1267, 1056, 995, 757, 690.

(Z)-3-Ethylidene-7-methylisobenzofuran-1(3H)-one (4be):^{26b} Light yellow solid; mp 77–81 °C, yield: 25% (35 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.51 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.24 (d, *J* = 7.4 Hz, 1H), 5.62 (q, *J* = 7.3 Hz, 1H), 2.68 (s, 3H), 2.01 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃): δ 167.2, 146.2, 139.9, 139.2, 133.9, 130.8, 122.1, 116.8, 103.2, 17.3, 11.1; IR (KBr, cm⁻¹) 3052, 2919, 2856, 1764, 1687, 1483, 1382, 1209, 999, 784, 692.

(Z)-3-Ethylidene-6-methylisobenzofuran-1(3H)-one (4ce):^{26c} Light yellow solid, mp 71–73 °C, yield 25% (35 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.67 (dt, *J* = 1.5, 0.8 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.48 (ddd, *J* = 8.0, 1.4, 0.5 Hz, 1H), 5.60 (q, *J* = 7.2 Hz, 1H), 2.48 (s, 3H), 2.02 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 167.2, 146.4, 139.8, 137.2, 135.5, 125.0, 124.6, 119.2, 103.1, 21.4, 11.1; IR (KBr, cm⁻¹) 3050, 2919, 2860, 1774, 1691, 1492, 1334, 1272, 1060, 991, 779, 763.

(Z)-3-Ethylidene-5-methylisobenzofuran-1(3H)-one (4de):^{26d} Light yellow liquid, mp 46–49 °C, yield 22% (31 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 7.9 Hz, 1H), 7.41 (s, 1H), 7.31 (d, *J* = 7.9 Hz, 1H), 5.63 (q, *J* = 7.2 Hz, 1H), 2.50 (s, 3H), 2.02 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 167.1, 146.4, 145.4, 140.0, 130.6, 124.9, 122.0, 119.6, 103.6, 22.1, 11.2; IR (KBr, cm⁻¹) 3049, 2917, 2860, 1776, 1691, 1618, 1270, 1052, 995, 773, 692.

(Z)-3-Ethylidene-5-methoxyisobenzofuran-1(3H)-one (4ee):^{26e} White solid, mp 99–101 °C, yield 27% (41 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.79 (dd, *J* = 8.3, 0.6 Hz, 1H), 7.04 (m, 2H), 5.65 (q, *J* = 7.2 Hz, 1H), 3.93 (s, 3H), 2.03 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 166.8, 164.9, 146.2, 142.0, 126.7, 117.6, 117.1, 103.9, 102.5, 55.8, 11.2; IR (KBr, cm⁻¹) 3008, 2964, 2917, 2842, 1766, 1606, 1486, 1297, 1110, 1051, 995, 773, 692.

(Z)-5-Chloro-3-ethylideneisobenzofuran-1(3H)-one (4fe): White solid, mp 116–118 °C, yield 20% (31 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.84 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 1.5 Hz, 1H), 7.49 (dd, *J* = 8.2, 1.6 Hz, 1H), 5.71 (q, *J* = 7.3 Hz, 1H), 2.05 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 165.9, 145.3, 141.0, 140.9, 129.9, 126.4, 122.8, 119.7, 105.6, 11.3; IR (KBr, cm⁻¹) 3089, 3062, 2958, 2921, 2854, 1774, 1608, 1432, 1324, 1265, 1068, 997, 829, 773; HRMS (ESI) *m/z*: calcd. for C₁₀H₇ClNaO₂ [*M* + Na]⁺ 217.0032, found 217.0031.

(Z)-3-Ethylidene-5-fluoroisobenzofuran-1(3H)-one (4ge): White solid; mp 90–92 °C, yield 19% (27 mg); ¹H NMR (400 MHz, CDCl₃) δ 7.90 (dd, *J* = 8.4, 4.8 Hz, 1H), 7.28 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.21 (td, *J* = 8.7, 2.2 Hz, 1H), 5.68 (t, *J* = 7.3 Hz, 1H), 2.04 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (400 MHz, CDCl₃) δ 168.0, 165.9, 165.5, 145.5, 145.5, 142.0, 141.9, 127.8, 127.6, 120.6, 117.8, 117.6, 106.5, 106.2, 105.6, 11.3; IR (KBr, cm⁻¹) 3089, 3066, 2952, 2923, 2860, 1783, 1766, 1621, 1589, 1477, 1448, 1288, 1054, 999, 775, 688; HRMS (ESI) *m/z*: calcd. for C₁₀H₇FNaO₂ [*M* + Na]⁺ 201.0328, found 201.0329.

(Z)-3-Ethylidene-5-phenylisobenzofuran-1(3H)-one (4he): Light yellow solid; mp 117–121 °C, yield: 12% (23 mg); ¹H NMR (500 MHz, CDCl₃) δ 7.94 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.79 (s, 1H), 7.71 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.66–7.62 (m, 2H), 7.54–7.49 (m, 2H), 7.48–7.44 (m, 1H), 5.75 (q, *J* = 7.2 Hz, 1H), 2.06 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃) δ 166.9, 147.7, 146.4, 140.2, 139.7, 129.0, 128.7, 128.6, 127.4, 125.5, 123.1, 117.9, 104.2, 11.2; IR (KBr, cm⁻¹) 3058, 3033, 2915, 2856, 1777, 1689, 1616, 1425, 1056, 995, 761, 694; HRMS (ESI) *m/z*: calcd. for C₁₆H₁₂NaO₂ [*M* + Na]⁺ 259.0735, found 259.0731.

(Z)-Methyl 3-Ethylidene-1-oxo-1,3-dihydroisobenzofuran-5-carboxylate (4ie): Light yellow solid; mp 157–160 °C, yield: 6% (11 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.32 (s, 1H), 8.17 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.96 (dd, *J* = 8.0, 0.7 Hz, 1H), 5.80 (q, *J* = 7.3 Hz, 1H), 4.01 (s, 3H), 2.07 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 166.1, 165.7, 145.8, 139.5, 135.6, 130.1, 127.5, 125.3, 121.1, 105.6, 52.8, 11.3; IR (KBr, cm⁻¹) 3058, 3039, 3008, 2956, 2921, 2853, 1780, 1722, 1591, 1440, 1430, 1249, 995, 754; HRMS (ESI) *m/z*: calcd. for C₁₂H₁₀NaO₄ [*M* + Na]⁺ 241.0477, found 241.0463.

(Z)-3-Ethylidenenaphtho[1,2-*c*]furan-1(3H)-one (4je):^{26b} Light yellow solid; mp 117–120 °C, yield: 19% (32 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.92 (d, *J* = 9.2 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.74 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.67–7.60 (m, 2H), 5.80 (q, *J* = 7.3 Hz, 1H), 2.11 (d, *J* = 7.3 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 167.2, 146.6, 140.1, 135.4, 133.5, 129.2, 128.8, 128.5, 127.3, 123.9, 118.5, 116.3, 105.6, 11.5; IR (KBr, cm⁻¹) 3066, 3054, 2950, 2904, 2850, 1758, 1685, 1315, 1178, 1087, 997, 964, 804, 794, 750.

(Z)-3-Ethylidenenaphtho[2,3-*c*]furan-1(3H)-one (4ke):^{26b} Light yellow solid; mp 119–122 °C, yield: 24% (40 mg); ¹H NMR (500 MHz, CDCl₃) δ 8.47 (s, 1H), 8.07 (s, 1H), 8.03 (d, *J* = 8.2 Hz, 1H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 5.79 (q, *J* = 7.2 Hz, 1H), 2.08 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃): δ 167.1, 146.3, 136.4, 133.9, 133.2, 130.0, 129.0, 128.5, 127.1, 126.6, 122.4, 118.3, 102.6, 11.1; IR (KBr, cm⁻¹) 3052, 2917, 2852, 1774, 1157, 1105, 997, 887, 777, 746.

■ ASSOCIATED CONTENT

● Supporting Information

Text, figures, tables, CIF file giving optimization details, NMR spectra for all new compounds, and crystallographic data for compound **4ie**. 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, see: (a) Barry, R. D. *Chem. Rev.* **1964**, *64*, 229. (b) Hill, R. A. In *Progress in the Chemistry of Organic Natural Products*; Springer Verlag: Wien, 1986; Vol. 49, pp 1–78.
- (2) For selected examples, see: (a) Whyte, A. C.; Gloer, J. B.; Scott, J. A.; Malloch, D. *J. Nat. Prod.* **1996**, *59*, 765. (b) Matsuda, H.; Shimoda, H.; Yoshikawa, M. *Bioorg. Med. Chem.* **1999**, *7*, 1445. (c) Zhang, H.; Matsuda, H.; Kumahara, A.; Ito, Y.; Nakamura, S.; Yoshikawa, M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4972. (d) Kurume, A.; Kamata, Y.; Yamashita, M.; Kawasaki, I.; Ohta, S.; Wang, Q.; Matsuda, H.; Yoshikawa, M. *Chem. Pharm. Bull.* **2008**, *56*, 1264. (e) Heynekamp, J. J.; Hunsaker, L. A.; Vander Jagt, T. A.; Royer, R. E.; Deck, L. M.; Vander Jagt, D. L. *Bioorg. Med. Chem.* **2008**, *16*, 5285. (f) Nozawa, K.; Yamada, M.; Tsuda, Y.; Kawai, K.-I.; Nakajima, S. *Chem. Pharm. Bull.* **1981**, *29*, 2491.
- (3) For reviews, see: (a) Napolitano, E. *Org. Prep. Proced. Int.* **1997**, *29*, 631. (b) Pal, S.; Chatare, V.; Pal, M. *Curr. Org. Chem.* **2011**, *15*, 782.
- (4) For selected examples, see: (a) Larock, R. C.; Doty, M. J.; Han, X. *J. Org. Chem.* **1999**, *64*, 8770. (b) Kadnikov, D. V.; Larock, R. C. *Org. Lett.* **2007**, *2*, 3643. (c) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936. (d) Peuchmaur, M.; Lisowski, V.; Gandreuil, C.; Maillard, L. T.; Martinez, J.; Hernandez, J.-F. *J. Org. Chem.* **2009**, *74*, 4158. (e) Sperança, A.; Godoi, B.; Pinton, S.; Back, D. F.; Menezes, P. H.; Zeni, G. *J. Org. Chem.* **2011**, *76*, 6789 and references therein. (f) Liao, H.-Y.; Cheng, C.-H. *J. Org. Chem.* **1995**, *60*, 3711. (g) Cherry, K.; Parrain, J.-L.; Thibonnet, J.; Duchêne, A.; Abarbri, M. *J. Org. Chem.* **2005**, *70*, 6669. (h) Cai, S.; Wang, F.; Xi, C. *J. Org. Chem.* **2012**, *77*, 2331. (i) Kavala, V.; Wang, C.-C.; Barange, D. K.; Kuo, C.-W.; Lei, P.-M.; Yao, C.-F. *J. Org. Chem.* **2012**, *77*, 5022. (j) Fan, X.; He, Y.; Cui, L.; Guo, S.; Wang, J.; Zhang, X. *Eur. J. Org. Chem.* **2012**, *673*. (k) Liu, L.; Hu, J.; Wang, X.-C.; Zhong, M.-J.; Liu, X.-Y.; Yang, S.-D.; Liang, Y.-M. *Tetrahedron* **2012**, *68*, 5391. (l) Fei, X.-D.; Ge, Z.-Y.; Tang, T.; Zhu, Y.-M.; Ji, S.-J. *J. Org. Chem.* **2012**, *77*, 10321. (m) Ge, Z.-Y.; Fei, X.-D.; Tang, T.; Zhu, Y.-M.; Shen, J.-K. *J. Org. Chem.* **2012**, *77*, 5736. (n) Yoo, W.-J.; Nguyen, T. V. Q.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 1.
- (5) (a) Godula, K.; Sames, D. *Science* **2006**, *312*, 67. (b) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507. (c) Yu, J. Q.; Shi, Z. J. *C-H Activation*; Springer: Berlin, Germany, 2010. (d) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (e) Engle, K. M.; Mei, T. S.; Wasa, M.; Yu, J. Q. *Acc. Chem. Res.* **2012**, *45*, 788. (f) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (g) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (h) Sun, C. L.; Li, B. J.; Shi, Z. J. *Chem. Rev.* **2011**, *111*, 1293. (i) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (j) Li, B. J.; Shi, Z. J. *Chem. Soc. Rev.* **2012**, *41*, 5588.
- (6) For reviews about Rh-catalyzed C–H activation/annulation reactions, see: (a) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (b) Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 11212. One review about carboxylate-directed C–H functionalization; see: (c) Shi, G.; Zhang, Y. *Adv. Synth. Catal.* **2014**, *356*, 1419. For several examples, see: (d) Ueura, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2007**, *72*, 5362. (e) Shimizu, M.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 3478. (f) Shi, X.-Y.; Renzetti, A.; Kundu, S.; Li, C.-J. *Adv. Synth. Catal.* **2014**, *356*, 723. (g) Cajaraville, A.; López, S.; Varela, J. A.; Sáa, C. *Org. Lett.* **2013**, *15*, 4576.
- (7) (a) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett.* **2007**, *9*, 1407. (b) Unoh, Y.; Hirano, K.; Satoh, T.; Miura, M. *Tetrahedron* **2013**, *69*, 4454. (c) Ackermann, L.; Pospech, J.; Graczyk, K.; Rauch, K. *Org. Lett.* **2012**, *14*, 930. (d) Chinnagolla, R. K.; Jegannathan, M. *Chem. Commun.* **2012**, *48*, 2030.
- (8) (a) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211. (b) Nandi, D.; Ghosh, D.; Chen, S.-J.; Kuo, B.-C.; Wang, N. M.; Lee, H. M. *J. Org. Chem.* **2013**, *78*, 3445.
- (9) For several examples about oxidative C–H olefination directed by a carboxylic group, see Rh: (a) Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 3024. (b) Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2010**, *12*, 5776. (c) Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 3024. (d) Iitsuka, T.; Schaal, P.; Hirano, K.; Satoh, T.; Bolm, C.; Miura, M. *J. Org. Chem.* **2013**, *78*, 7216. Ru: (e) Ackermann, L.; Pospech, J. *Org. Lett.* **2011**, *13*, 4153. (f) Ueyama, T.; Mochida, S.; Fukutani, T.; Hirano, K.; Satoh, T. *Org. Lett.* **2011**, *13*, 706.
- (10) Guimond, N.; Gouliaras, C.; Fagnou, K. *J. Am. Chem. Soc.* **2011**, *133*, 6449.
- (11) During the preparation of our manuscript, we noticed that a similar paper about Rh(III)-catalyzed C–H activation/annulation of pivaloyl hydroxamate with vinyl esters as acetylene equivalent had appeared; see: Webb, N. J.; Marsden, S. P.; Raw, S. A. *Org. Lett.* **2014**, *16*, 4718.
- (12) (a) Yu, J.-Y.; Kuwano, R. *Angew. Chem., Int. Ed.* **2012**, *48*, 7217. (b) Matsuura, Y.; Tamura, M.; Kochi, M.; Sato, M.; Chatani, N.; Kakiuchi, F. *J. Am. Chem. Soc.* **2007**, *129*, 9858. (c) Hatamoto, Y.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2004**, *6*, 4623. (d) Meng, L.; Liu, C.; Zhang, W.; Zhou, C.; Lei, A. *Chem. Commun.* **2014**, *50*, 1110 and references therein.
- (13) For catalytic addition of carboxylic acid to alkynes for the formation of enol esters, see: (a) Philippot, K.; Devanne, D.; Dixneuf, P. H. *J. Chem. Soc., Chem. Commun.* **1990**, 1199. (b) Neveux, M.; Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc., Perkin Trans 1* **1991**, 1197. (c) Doucet, H.; Höfer, J.; Bruneau, C.; Dixneuf, P. H. *J. Chem. Soc., Chem. Commun.* **1993**, 850. (d) Doucet, H.; Martin-Vaca, B.; Bruneau, C.; Dixneuf, P. H. *J. Org. Chem.* **1995**, *60*, 7247. (e) Doucet, H.; Derrien, N.; Kabouche, Z.; Bruneau, C.; Dixneuf, P. H. *J. Organomet. Chem.* **1997**, *551*, 151.
- (14) Although the reaction performed in toluene/*tert*-amyl alcohol (2:1) gave slightly lower yield, the transformation seems much cleaner in TLC than the reactions performed in other solvents.
- (15) For a review of the roles of bases in transition-metal-mediated organic reactions, see: Ouyang, K.; Xi, Z. *Acta Chim. Sin.* **2013**, *71*, 13.
- (16) KI may cause the in situ ligand exchange, see: Maetani, S.; Fukuyama, T.; Ryu, I. *Org. Lett.* **2013**, *15*, 2754.
- (17) For details about the reaction optimization, see the Supporting Information.
- (18) The configuration of the double bonds in product **4** was confirmed through X-ray crystal structure analysis of **4ie** (CCDC 1024384); see the Supporting Information.
- (19) A trace amount of **3aa** may be derived from the hydrolysis of **5**, followed by the C–H activation/annulation of benzoic acid with **5**.
- (20) (a) Lobell, M.; Schneider, M. P. *Synthesis* **1994**, 375. (b) Sabel, A.; Smidt, J.; Jira, R.; Prigge, H. *Chem. Ber.* **1969**, *102*, 2939.
- (21) Lemma, A.; Ellern, A.; Bakac, A. *Inorg. Chem.* **2003**, *42*, 3662.
- (22) (a) Kumar, M. R.; Irudayanathan, F. M.; Moon, J. H.; Lee, S. *Adv. Synth. Catal.* **2013**, *355*, 3221. (b) Müller, E. *Ber. Deutsch. Chem. Ges.* **1909**, *42*, 423. (c) Nandi, D.; Ghosh, D.; Chen, S.-J.; Kuo, B.-C.; Wang, N. M.; Lee, H. M. *J. Org. Chem.* **2013**, *78*, 3445. (d) Ge, Z.-Y.; Fei, X.-D.; Tang, T.; Zhu, Y.-M.; Shen, J.-K. *J. Org. Chem.* **2012**, *77*, 5736.
- (23) (a) Cherry, K.; Parrain, J.-L.; Thibonnet, J.; Duchêne, A.; Abarbri, M. *J. Org. Chem.* **2005**, *70*, 6669. (b) Kavala, V.; Wang, C.-C.; Barange, D. K.; Kuo, C.-W.; Lei, P.-M.; Yao, C.-F. *J. Org. Chem.* **2012**, *77*, 5022. (c) Cai, S.; Wang, F.; Xi, C. *J. Org. Chem.* **2012**, *77*, 2331. (d) Chobanian, H. R.; Liu, P.; Chioda, M. D.; Guo, Y.; Lin, L. S.

Tetrahedron Lett. **2007**, 48, 1213. (e) Bacon, R. G. R.; Murray, J. C. F. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1267. (f) Peuchmaur, M.; Lisowski, V.; Gandreuil, C. I.; Maillard, L. T.; Martinez, J.; Hernandez, J.-F. *J. Org. Chem.* **2009**, 74, 4158. (g) Khan, K.; Ahmed, S.; Khan, Z.; Rani, M.; Perveen, S.; Choudhary, M.; Atta-ur-Rahman. *Lett. Org. Chem.* **2005**, 2, 532.

(24) Spassov, S. L.; Atanassova, I. A.; Haimova, M. A. *Org. Magn. Reson.* **1984**, 22, 194.

(25) Larock, R. C.; Hightower, T. R. *J. Org. Chem.* **1993**, 58, 5298.

(26) (a) Negishi, E.-I.; Copéret, C.; Ma, S.; Mita, T.; Sugihara, T.; Tour, J. M. *J. Am. Chem. Soc.* **1996**, 118, 5904. (b) Danoun, G.; Mamone, P.; Gooßen, L. *J. Chem.—Eur. J.* **2013**, 19, 17287. (c) Novák, P.; Correa, A.; Gallardo-Donaire, J.; Martin, R. *Angew. Chem., Int. Ed.* **2011**, 50, 12236. (d) Ciattini, P. G.; Mastropietro, G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1993**, 34, 3763. (e) Ortar, G.; Schiano Moriello, A.; Morera, E.; Nalli, M.; Di Marzo, V.; De Petrocellis, L. *Bioorg. Med. Chem. Lett.* **2013**, 23, 5614.