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Synthesis of Isocoumarins via Silver(I)-Mediated Annulation of Enol Esters

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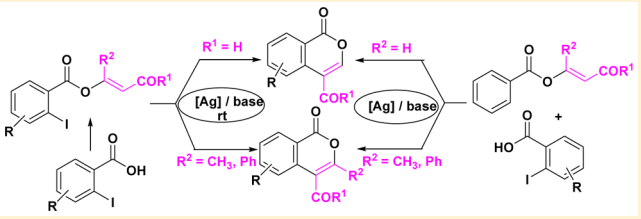
Supporting Information

ABSTRACT: Silver-mediated annulation of 2-iodo enol esters leading to 4- and 3,4-substituted isocoumarins was accomplished selectively at room temperature. Coupling of 2-iodo benzoic acids with enolates that were produced in situ from the simple esters was also performed to produce isocoumarins under analogous reaction conditions. Owing to the mildness of the current protocol, 4-acyl 3-substituted isocoumarins were efficiently produced without any deacylation.



INTRODUCTION

Isocoumarin, a privileged molecular skeleton, is present in numerous natural as well as synthetic products that exhibit a wide range of pharmacological properties including antifungal, antitumor, antiallergic, antimicrobial, anti-inflammatory, antidiabetic, phytotoxic, anticancer, and inhibitory activities.[1−3] Isocoumarins are also endowed as a pivotal intermediate in the synthesis of several other compounds such as isoquinolines, isochromenes, and isocarbostyrils.[4] These physiochemical features have spurred considerable interest in developing new methods with enhanced scope, generality, and cost effectiveness for their synthesis. Of the reported methods, the transition metal (TM) mediated Sonogashira type coupling of terminal alkynes with halo carboxylic acids or their equivalents, followed by *6-endo-dig* cyclization, has been strenuously developed and recognized as an attractive strategy to construct the isocoumarin ring.[5] Besides, some other methods that involve the oxidative annulation of the carboxylic acid with alkynes through C−H activation reaction using Ru-, Rh-, and Ir-complexes have been reported.[6] Though these methods are of high synthetic value, multistep access to generate the starting material, stoichiometric use of toxic and expensive TM catalyst, and high temperature above 100 °C often limit their application. Moreover, some of these reactions have reduced substrate scope and also result in a number of undesired side products (e.g., phthalides).[7] Consequently, Cu-catalyzed cross-coupling of 2-halobenzoic acids or their derivatives with 1,3-dicarbonyl compounds have thus appeared as a potential alternate strategy to achieve isocoumarins.[8] For instance, Fan and his co-workers prepared 3- and 3,4-substituted isocoumarins through a Cu^{I}-catalyzed tandem reaction of 2-bromobenzoates with acyclic 1,3-diones, followed by annulation.[9a] Xi et al. also adopted a similar annulation strategy for the synthesis of 3-substituted coumarins.[9b] Indeed, these reactions proceed with the initial Cu-catalyzed C-arylation of 1,3-diketone (Hurtley reaction), followed by annulation reaction. Evidently, deacylation occurs through a four-membered ring with C−C and C−O bond cleavage to give the 3-substituted isocoumarins. Yao and co-workers also reported a Cu-catalyzed tandem C−C/C−O coupling reaction of 2-iodo-*N*-phenyl-benzamides with 1,3-diketones to produce 3-substituted isocoumarins.[9c] Notably, Shen et al. reported a proficient ligand assisted Cu-catalyzed protocol for the synthesis of 3-substituted isocoumarins from the intramolecular C−C coupling and rearrangement of 1-(2-halophenyl)-1,3-diones.[9d]

Despite these formidable advances, limited investigations have been aimed particularly at the synthesis of 4-substituted isocoumarins, although they possess significant antiangiogenic, antitumor, and antibiotic activities against bacteria, and plant pathogenic fungi.[10] Notably, Vilsmeier reaction of homophthalic acid, followed by hydrolysis, has been mostly employed to access 4-substituted isocoumarins,[11] though few 4-alkyl/aryl-substituted isocoumarins have been prepared in the presence of Pd catalyst.[12] Nevertheless, restricted substrate scope, inconvenient reaction procedures, and multistep syntheses of the reagents often precluded their widespread use. A general catalytic method to various 4-substituted isocoumarins is, therefore, demanding and would also serve to provide an excellent opportunity to accelerate biological and biosynthetic studies of these valuable compounds.[13] Furthermore, Ag-catalyzed coupling reactions are relatively less literature precedented, though stoichiometric amounts of Ag(I) salts are uniquely used as co-oxidant for Pd-, Au-, Cu-, Rh-, Ru-, and Pt-catalyzed reactions.[14] In continuation of our effort toward the synthesis of newer heterocycles,[15] we here report a novel Ag-mediated efficient method for the selective synthesis of 4-substituted isocoumarins from readily accessible enol esters under mild reaction conditions even at room temperature. This method is also useful to enable 3,4-disubstituted isocoumarins in good yield. Furthermore, the first example of a silver-mediated reaction of the *o*-halo benzoic

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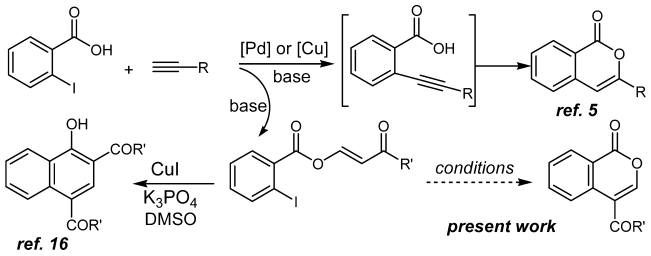
acid and enol ester leading to isocoumarins through the C-arylation of enolates, followed by annulation, is also presented.

RESULTS AND DISCUSSION

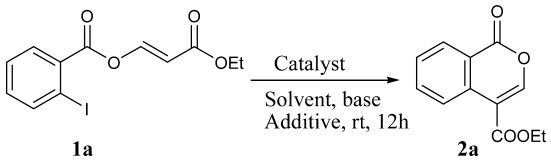
In contrast to the previous methods for the preparation of 3-substituted coumarins (Scheme 1),[5,16] we speculated that

Scheme 1. Synthetic Strategy for the 4-Substituted Isocoumarin



suitably functionalized enol esters would undergo transition-metal-catalyzed intramolecular cyclization to produce 4-substituted isocoumarins selectively. Consequently, a number of enol esters were prepared by the reaction of esters of propiolic acid with *o*-halo benzoic acids following the similar procedure reported earlier.[16] To study the annulation reaction, 2-(ethoxycarbonyl)vinyl 2-iodobenzoate (**1a**) was chosen as a model substrate. Recently, we observed that treatment of **1a** with CuI in the presence of base (e.g., K_3PO_4) produces substituted α-naphthol,[16] and no trace of isocoumarin was observed. Replacement of CuI by $Pd(OAc)_2$ (5 mol %) was also found to be unsuccessful. However, with the addition of Ag_2CO_3 (1 equiv) as co-oxidant, fascinatingly, the desired 4-substituted isocoumarin **2a** was produced (15% yield) along with the decomposition of the remaining starting material. Inspired by this result, we believed that silver salts might be exclusively responsible for the annulation reaction.[17] Thus, we turned our attention toward the use of silver salt as the only catalyst for the above transformation, though no report on such a type of silver-mediated *C*-arylation is yet the precedent. Optimization study was performed by varying the catalyst, solvent, base, etc., to develop a suitable condition for the annulation reaction (Table 1). Among the screened solvents (e.g., THF, toluene, DMF, DCE, CH_3CN, 1,4-dioxane, etc.), CH_3CN was served as the most efficient solvent to produce the highest yield of **2a**. AgOAc (1 equiv) showed to be the best catalyst to enable the highest yield of **2a** (95%) when compared with other catalysts such as Ag_2O, Ag_2CO_3, and $AgNO_3$ during the catalyst screening. Ag_2O also results in 79% of isocoumarin at room temperature.

Table 1. Optimization of Reaction Conditions[a]



1a **2a**

entry	catalyst (mol %)	solvent	base	additive	yield (%)
1	CuI	toluene	K_3PO_4		0[16]
2	$Pd(OAc)_2$ (5)	toluene	K_2CO_3		0
3	$Pd(OAc)_2$ (5)	CH_3CN	K_3PO_4	Ph_3P	0
4	$Pd(OAc)_2$ (5)	CH_3CN	NaOAc		0
5	$Pd(OAc)_2$ (5)	CH_3CN	DMAP	Ag_2CO_3	15
6	Ag_2CO_3 (100)	CH_3CN	DMAP		38
7	Ag_2O (100)	CH_3CN	DMAP		79
8	AgOAc (100)	CH_3CN	Py		56
9	AgOAc (100)	CH_3CN	Et_3N		34
10	AgOAc (100)	CH_3CN	K_2CO_3		15
11	AgOAc (100)	CH_3CN	NaOAc		18
12	**AgOAc (100)**	**CH_3CN**	**DMAP**		**95**
13	AgOAc (50)	CH_3CN	DMAP		66
14	AgOAc (70)	CH_3CN	DMAP		80
15	AgOAc (100)	THF	DMAP		38
16	AgOAc (100)	DMF	DMAP		42
17	AgOAc (100)	DCE	DMAP		78
18	AgOAc (100)	1,4-dioxane	DMAP		26
19	AgOAc (100)	toluene	DMAP		33
20	AgOAc (100)	H_2O	DMAP		NR
21	Ag_2O (30)	CH_3CN	DMAP	$K_2S_2O_8$	76
22	Ag_2CO_3 (30)	CH_3CN	DMAP	$NaBO_3{\cdot}4H_2O$	0
23	Ag_2O (30)	CH_3CN	DMAP	oxone	0
24	AgOAc (30)	CH_3CN	DMAP	$K_2S_2O_8$	45
25	AgOAc (100)	EtOH	DMAP		7
26		CH_3CN	DMAP		<10
27	AgOAc (100)	CH_3CN			15

[a]Reaction conditions: enol ester **1a** (50 mg, 0.14 mmol), catalyst, base (1.2 equiv), additive (1 equiv), solvent (2 mL), rt, 12 h.

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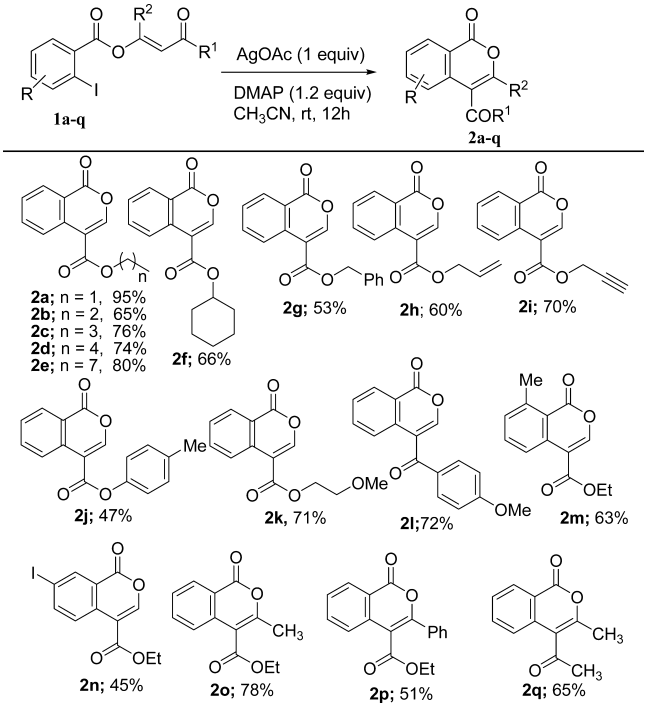
To reduce the catalyst consumption, several oxidants were used to perform the reaction. Notably, when 1.1 equiv of $K_2S_2O_8$ was used along with 0.3 equiv of Ag_2O and base (1.2 equiv), 76% of **2a** was isolated. However, AgOAc (0.3 equiv) in the presence of 1 equiv of $K_2S_2O_8$ was observed to be less efficient (entry 24). Next, we investigated the effect of different bases in CH_3CN in the presence of AgOAc. To our delight, 4-dimethylaminopyridine (DMAP) was observed to be most effective to catalyze the reaction, whereas other bases such as pyridine, Et_3N, K_2CO_3, and NaOAc were substantially less useful. Significantly, in the absence of the base, only a small amount of product (15%) was produced with the recovery of remaining enol ester. When the reaction was performed in the absence of Ag catalyst, decomposition of starting material occurs, and 10% of the product **2a** was isolated. Furthermore, we observed that the reaction does not require any dedicated inert atmosphere and, more importantly, it completes at room temperature in the presence of atmospheric air over a period of 12 h. Notably, under the optimum reaction conditions (1 equiv of AgOAc, 1.2 equiv of DMAP in acetonitrile at rt), **1a** did not undergo 5-exo-dig cyclization and 5-membered phthalide was not formed.

Next, we extended the utility of the protocol for the annulation of various enol esters under the optimized reaction conditions. As shown in Scheme 2, enol esters, prepared from

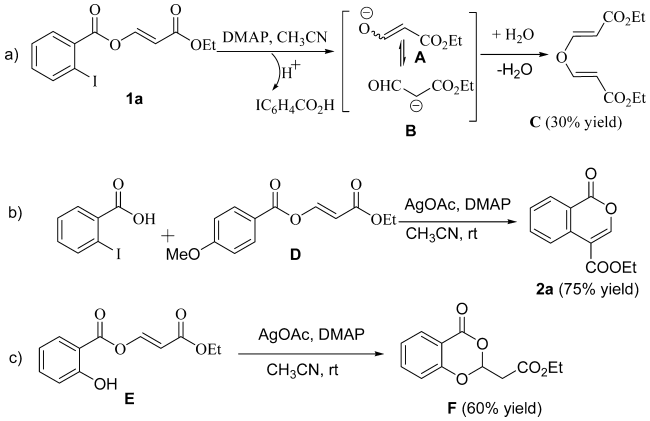
Scheme 2. Synthesis of Isocoumarins from 2-Iodo Enol Esters



several propiolates, underwent intramolecular cyclization by offering 4-substituted coumarins in moderate to good yields. When the (*E*)-2-(ethoxycarbonyl)vinyl 2-bromobenzoate was treated under similar reaction conditions, the reaction became sluggish with the production of **2a** over a period of 36 h (40% yield). Similarly, as expected, the less reactive (*E*)-2-(ethoxycarbonyl)vinyl 2-chlorobenzoate did not produce **2a** at room temperature over a period of 12 h. However, raising the temperature to 80 °C, **2a** was produced hitherto in low yield (15%). Pleasantly, annulation of other *o*-iodo vinyl benzoates having variable chain lengths occurred and isocoumarins (**2b**–**2e**) were produced in good yield (65–80%). The keto functionality in the enol ester was also found to be tolerant to produce the desired isocoumarins (**2l**, **2q**) in moderate to good yield. Other substituents (such as iodo and methyl groups) to the aromatic ring were also lenient to the reaction conditions by producing the corresponding isocoumarins **2m** and **2n** in 63% and 45% yield, respectively. Most importantly, the current protocol activates the C–I bond ortho to the carbonyl group for the cyclization, whereas other C–I bonds remain unaffected. Furthermore, under the same reaction conditions, 3,4-disubstituted isocoumarins (**2o**–**2q**) were also obtained in moderate to good yield.

On the basis of some control experiments (Scheme 3), a hypothesis was formulated to explain these results, although no

Scheme 3. Control Experiments for Mechanism



compelling evidence had yet been gathered. Notably, addition of 1 equiv of TEMPO to the reaction mixture did not lower the yield significantly (79% isolated yield of **2a**), which excludes the involvement of a radical pathway in the above transformation. The reaction of enol ester **1a** with DMAP in the absence of the catalyst, followed by acidification of the reaction mixture, led to the *o*-iodobenzoic acid and bis(trans-2-ethoxycarbonylvinyl) ether (**C**).[16] Furthermore, the reaction of the *o*-iodobenzoic acid with 2-(ethoxycarbonyl)vinyl 4-methoxybenzoate (**D**) also produces **2a**, albeit in reduced yield (75%). Besides, when enol ester such as **E** was treated under similar reaction conditions, nucleophilic attack occurs to the aldehyde group of **B** with the formation of benzodioxanone[18] **F**. These observations suggest that the enol ester **1a** initially reacts with DMAP to produce the enolate (e.g., **A** which rearranges to **B**) along with the intermediate **I** (Scheme 4). Subsequently, *C*-arylation may occur through oxidative addition of silver catalyst (e.g., **II**), by producing the intermediate **III**. Evidently, analogous Cu-catalyzed *C*-arylation is endowed with literature precedent,[16,19] and the potential of the Ag catalyst in the above *Csp2*–*Csp3* bond formation is not well exploited.[20] Upon enolization (e.g., **IV**) and subsequent nucleophilic attack forms the corresponding isocoumarin (e.g., **2a**) selectively.

Finally, from the control experiments, we recognized that our new method could be employed for the straightforward synthesis of isocoumarins from the reaction of an *o*-halo benzoic acid and simple enol esters (Table 2). Thus, when *o*-iodobenzoic acids[21] with different substituents were treated with the readily prepared enol ester of benzoic acid (**4a**), 4-

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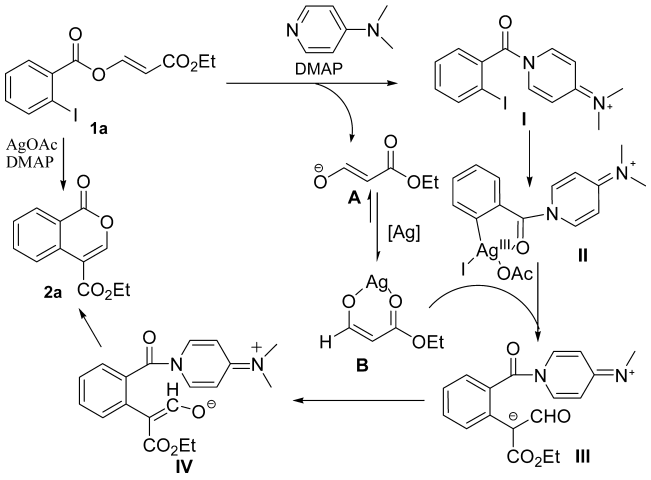
Scheme 4. Plausible Mechanism for the Synthesis of 2a from 1a



substituted isocoumarins were produced smoothly in good yield (see Scheme 5 for possible mechanism). Consequently, 3-methyl-4-ethylcarboxylates (entries 5−7) were achieved under the similar reaction conditions from *o*-iodobenzoic acids in moderate yield. Notably, earlier work[9] on coupling of the 2-halo benzoic acid with dicarbonyl compounds in the presence of CuI was reported to be unsuitable to afford 3-substituted 4-acyl isocoumarins. Regrettably, deacylation occurs unambiguously through a four-membered cyclic intermediate and 3-substituted isocoumarins are produced exclusively. However, when we treated *o*-iodobenzoic acid with the enol ester **4c**, owing to the mild reaction conditions of the current method, 3-substituted 4-acylated isocoumarins (**2q**, **5d**−**g**) were produced smoothly without any deacylation. In comparison to our earlier report on Cu-catalyzed *α*-naphthol synthesis,[16] it may be presumed that the silver catalyst is more selective toward the *C*-arylation than the *C*-carbonylation reaction, and hence, isocoumarin are formed exclusively.

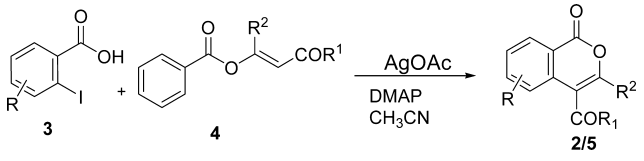
CONCLUSION

In summary, we have developed a simple protocol for the synthesis of less precedent 4-substituted isocoumarins under very mild reaction conditions simply by switching the catalyst from Cu to Ag. The potential of the Ag catalysis in the *Csp2*−*Csp3* bond formation reaction was also recognized exclusively. An alternate and complementary silver-mediated strategy for the synthesis of isocoumarins from the reaction of easily accessible enol esters and *o*-halo benzoic acid was also demonstrated. The current method is found to be simple and mild enough to produce 4- and 3,4-substituted isocoumarins selectively. Unlike earlier methods, deacylation did not occur under this reaction condition. Further synthetic application of the above methodology toward the total synthesis of natural products such as sescandelin, oosponol, and antibiotic AGI-7 is underway in our laboratory.

EXPERIMENTAL SECTION

General Information. All reactions were carried out in a closed round-bottom flask. All commercial reagents were used without purification, and all solvents were reaction grade. The reactions were monitored by TLC, and the residue was chromatographed on silica gel (Rankem, India, Mesh 60−120), using an ethyl acetate−petroleum ether (60−80 °C) mixture as eluent. All the melting points are uncorrected and measured in sulfuric acid bath. All NMR spectra were recorded on a 400 MHz (for ^{1}H NMR, 100 MHz for ^{13}C NMR) NMR spectrometer, and chemical shifts were expressed in δ units relative to the TMS signal as internal reference in $CDCl_3$. Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet, when multiplicity is complex) for ^{1}H NMR. Coupling constants, *J* were reported in Hz. IR spectra were recorded by an FTIR

Table 2. Isocoumarins Synthesis from *o*-Iodobenzoic Acid and Enol Esters[a]



Entry	acid	enol ester	Isocoumarin	Yield (%)
1	3a	4a	2a	79
2	3b	4a	2n	42
3	3c	4a	5a	63
4	3d	4a	2m	48
5	3a	4b	2o	65
6	3b	4b	5b	48[b]
7	3c	4b	5c	55[b]
8	3a	4c	2q	47[b]
9	3b	4c	5d	45[b]
10	3c	4c	5e	41[b]
11	3d	4c	5f	49[b]
12	3e	4c	5g	40[b]

[a]Reaction conditions: enol ester **4** (50 mg), *o*-iodobenzoic acid (1 equiv), AgOAc (1 equiv), DMAP (2 equiv), in 2 mL of CH_3CN, rt for 12 h. [b]50 °C for 12 h.

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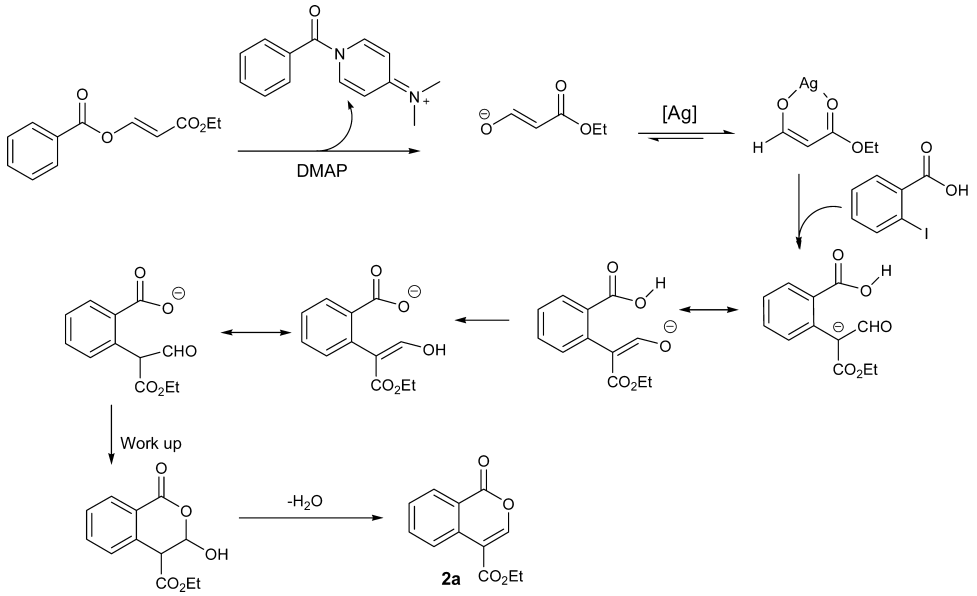
Scheme 5. Plausible Mechanism for the Synthesis of 2a from 3a



spectrometer (IR Affinity 1S W/L with quest ATR). Catalyst composition was analyzed via inductively coupled plasma optical emission spectroscopy (ICP-OES). From ICP-OES analysis, it was found that the weight percent of silver in AgOAc is >99.91%. Other impurities such as Cu (0.017%), Fe (0.06%), and Ni (0.01%) are present in negligible amounts and expectedly did not contribute to the transformation.

General Procedure for Preparation of Enol Esters[16] (Method A). A mixture of 2-iodo acid (1.0 equiv), alkyl propiolate (1.1 equiv), and pyridine (2.0 equiv) in 15 mL of toluene was stirred at room temperature. After 12 h, the reaction mixture was diluted with ethyl acetate (15 mL), followed by 1 N HCl (10 mL) solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over brine, anhydrous Na_2SO_4, and then evaporated under reduced pressure. The crude residue was purified by column chromatography over silica gel using a mixture of petroleum ether and ethyl acetate as eluent to give the desired enol esters.

General Procedure for Preparation of α-Substituted Enol Esters (Method B). Synthesis of α-substituted enol esters was achieved by following the slightly modified procedure reported by Mohrig and co-workers.[22] To a stirred solution of 2-iodo acid (500 mg, 2.02 mmol) in 5 mL of dichloromethane was added oxalyl chloride (0.5 mL) at room temperature under a nitrogen atmosphere. Then, 2 drops of DMF were added to initiate the reaction. The resulting solution was stirred at room temperature for 8 h, and then solvent was removed under reduced pressure. To the resulting slurry, dry acetonitile (2 mL) was added. In another round-bottom flask, 1,3-dicarbonyl compound (1 equiv) was treated with DBU (1.2 equiv) in 8 mL of dry acetonitrile over a period of 15 min at room temperature. This resulting solution was then added to the previously prepared acid chloride solution with the help of a syringe over a period of 15 min. After 12 h, the reaction mixture was diluted with ethyl acetate (15 mL), followed by 1 N HCl (10 mL) solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over brine, anhydrous Na_2SO_4, and then evaporated under reduced pressure. The crude residue was purified by column chromatography over silica gel using a mixture of petroleum ether and ethyl acetate as eluent to give the desired substituted enol esters.

General Procedure for Preparation of Enol Esters from Acid Chlorides (Method C). To a stirred solution of 1,3-dicarbony compounds (1 equiv) and DBU (1.2 equiv) in 8 mL of dry acetonitrile was added benzoyl chloride (500 mg, 3.57 mmol) dropwise over a period of 15 min at room temperature. After 12 h, the reaction mixture was then diluted with ethyl acetate (15 mL), followed by 1 N HCl (10 mL) solution. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over brine, anhydrous Na_2SO_4, and then evaporated under reduced pressure. The crude residue was purified by column chromatography over silica gel using a mixture of petroleum ether and ethyl acetate as eluent to give the desired substituted enol esters.

*(E)-2-(ethoxycarbonyl)vinyl 2-Iodobenzoate[16] (**1a**).* Following method A, compound **1a** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and ethyl propiolate (216 mg, 2.21 mmol) as a colorless solid (590 mg, 85% yield); mp 77−78 °C; IR (KBr) 3053, 2964, 2873, 1748, 1683, 1632, 1555, 1535, 1510, 1468, 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, 1H, J = 12.4 Hz), 8.09 (dd, 1H, J_1 = 8.0 Hz, J_2 = 0.8 Hz), 7.97 (dd, 1H, J_1 = 7.6 Hz, J_2 = 1.6 Hz), 7.52−7.46 (m, 1H), 7.28−7.23 (m, 1H), 5.92 (d, 1H, J = 12.4 Hz), 4.26 (q, 2H, J = 7.2 Hz), 1.34 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 161.9, 149.5, 142.0, 133.9, 132.0, 131.9, 128.1, 107.0, 90.1, 60.6, 14.2. MS (ESI, + ve) m/z (relative intensity) 369.02 ($[M + Na]^+$, 100%).

*(E)-2-(Propoxycarbonyl)vinyl 2-Iodobenzoate[16] (**1b**).* Following method A, compound **1b** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and propyl propiolate (248 mg, 2.21 mmol) as a colorless solid (566 mg, 78% yield); mp 74−75 °C; IR (KBr) 3090, 2966, 2885, 1755, 1718, 1653, 1581, 1464, 1430, 1389, 1285, 1232, 1062, 1032, 1011 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, 1H, J = 12.8 Hz), 8.08 (dd, 1H, J_1 = 8 Hz, J_2 = 0.8 Hz), 7.97 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.6 Hz), 7.50−7.45 (m, 1H), 7.28−7.22 (m, 1H), 5.92 (d, 1H, J = 12.4 Hz), 4.15 (t, 2H, J = 6.8 Hz), 1.76−1.67 (m, 2H), 0.99 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 161.8, 149.4, 142.1, 134.0, 131.9, 128.1, 107.0, 95.2, 66.2, 22.0, 10.4. MS (ESI, + ve) m/z (relative intensity) 742.93 ($[2M + Na]^+$, 100%), 382.90 ($[M + Na]^+$, 80%).

*(E)-2-(Butoxycarbonyl)vinyl 2-Iodobenzoate[16] (**1c**).* Following method A, compound **1c** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and butyl propiolate (279 mg, 2.21 mmol) as a colorless solid (573 mg, 76% yield); mp 76−78 °C; IR (KBr) 3087, 2953, 2868, 1748, 1698, 1654, 1578, 1459, 1316, 1268, 1231, 1192, 1133, 1011 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, 1H, J = 12.8 Hz), 8.07 (t, 1H, J = 7.2 Hz), 7.97 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.6 Hz), 7.50−7.45 (m, 1H), 7.28−7.22 (m, 1H), 5.91 (d, 1H, J = 12.4 Hz), 4.19 (t, 1H, J = 6.8 Hz), 1.72−1.63 (m, 2H), 1.46−1.39 (m, 2H), 0.96 (t, 3H, J = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.03, 161.8, 149.4, 142.1, 134.0, 131.9, 128.1, 107.0, 95.2, 64.5, 30.6, 19.1,

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13.7. MS (ESI, + ve) m/z (relative intensity) 396.97 ([M + Na]$^+$, 100%).

(E)-2-((Pentyloxy)carbonyl)vinyl 2-Iodobenzoate[16] ***(1d)***. Following method A, compound **1d** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and pentyl propiolate (310 mg, 2.211 mmol) as a colorless liquid (563 mg, 72% yield); IR 3090, 2953, 2888, 2856, 1749, 1702, 1657, 1577, 1460, 1431, 1310, 1294, 1266, 1231, 1190, 1169, 1131, 1033, 1010 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, 1H, J = 12.4 Hz), 8.08 (dd, 1H, J_1 = 8.2 Hz, J_2 = 1.2 Hz), 7.97 (dd, 1H, J_1 = 8.0 Hz, J_2 = 1.6 Hz), 7.50−7.45 (m, 1H), 7.28−7.22 (m, 1H), 5.92 (d, 1H, J = 12.8 Hz), 4.19 (m, 2H), 1.72−1.65 (m, 2H), 1.40−1.33 (m, 4H), 0.96−0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 161.8, 149.4, 142.1, 134.0, 131.9, 131.9, 128.1, 107.0, 95.2, 64.8, 28.3, 28.0, 22.3, 13.9. MS (ESI, + ve) m/z (relative intensity) 411.00 ([M + Na]$^+$, 100%), 799.00 ([2M + Na]$^+$, 80%).

(E)-2-((Octyloxy)carbonyl)vinyl 2-Iodobenzoate[16] ***(1e)***. Following method A, compound **1e** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and octyl propiolate (372 mg, 2.21 mmol) as a colorless liquid (590 mg, 68% yield); IR 3089, 2941, 2925, 2850, 1749, 1703, 1657, 1577, 1464, 1432, 1314, 1267, 1230, 1193, 1132, 1107, 1031, 1010 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, 1H, J = 12.4 Hz), 8.04 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 7.93 (dd, 1H, J_1 = 8 Hz, J_2 = 1.6 Hz), 7.47−7.41 (m, 1H), 7.24−7.18 (m, 1H), 5.88 (d, 1H, J = 12.4 Hz), 4.15 (t, 2H, J = 6.8 Hz), 1.69−1.61 (m, 2H), 1.36−1.24 (m, 10H), 0.85 (t, 3H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 161.8, 149.4, 142.1, 134.0, 132.0, 131.8, 128.1, 107.0, 95.2, 64.8, 31.8, 29.2, 29.2, 28.6, 25.9, 22.6, 14.1. MS (ESI, + ve) m/z (relative intensity) 453.09 ([M + Na]$^+$, 100%).

(E)-2-((Cyclohexyloxy)carbonyl)vinyl 2-Iodobenzoate[16] ***(1f)***. Following method A, compound **1f** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and cyclohexyl propiolate (336 mg, 2.21 mmol) as a yellow oil (588 mg, 73% yield); IR 3282, 2913, 2845, 1751, 1718, 1683, 1642, 1577, 1457, 1429, 1370, 1221 cm.$^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, 1H, J = 12.4 Hz), 8.05 (dd, 1H, J = 8 Hz), 7.94 (dd, 1H, J = 8 Hz), 7.49−7.43 (m, 1H), 7.26−7.20 (m, 1H), 5.89 (d, 1H, J = 12.4 Hz), 4.90−4.82 (m, 1H), 1.92−1.86 (m, 2H), 1.77−1.72 (m, 2H), 1.57−1.23 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 161.9, 149.2, 142.0, 134.0, 131.9, 131.9, 128.1, 107.5, 95.2, 72.9, 31.6, 25.3, 23.7. MS (ESI, + ve) m/z (relative intensity) 423.01 ([M + Na]$^+$, 100%).

(E)-2-((Benzyloxy)carbonyl)vinyl 2-Iodobenzoate[16] ***(1g)***. Following method A, compound **1g** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and benzyl propiolate (354 mg, 2.21 mmol) as a colorless liquid (658 mg, 80% yield); IR 3086, 3053, 2952, 1752, 1718, 1654, 1580, 1455, 1272, 1230, 1090, 1007 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, 1H, J = 12.4 Hz), 8.08 (dd, 1H, J_1 = 8 Hz, J_2 = 0.8 Hz), 7.97 (dd, 1H, J_1 = 7.6 Hz, J_2 = 1.6 Hz), 7.47 (t, 1H, J = 0.8 Hz), 7.43−7.37 (m, 5H), 7.28−7.24 (m, 1H), 5.98 (d, 1H, J = 12.4 Hz), 5.25 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.8, 149.9, 142.1, 135.7, 134.1, 132.0, 131.7, 128.6, 128.3, 128.3, 128.2, 106.7, 95.3, 66.4. MS (ESI, +ve) m/z (relative intensity) 838.84 ([2M + Na]$^+$, 100%), 430.90 ([M + Na]$^+$, 50%).

(E)-2-((Allyloxy)carbonyl)vinyl 2-Iodobenzoate[16] ***(1h)***. Following method A, compound **1h** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and allyl propiolate (243 mg, 2.21 mmol) as a colorless liquid (512 mg, 71% yield); IR 3086, 2916, 2840, 1754, 1718, 1654, 1580, 1429, 1273, 1230, 1105, 1006 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, 1H, J = 12.4 Hz), 8.08 (d, 1H, J = 8.0 Hz), 7.97 (dd, 1H, J_1 = 8 Hz, J_2 = 1.6 Hz), 7.49 (dd, 1H, J_1 = 11.2 Hz, J_2 = 0.8 Hz), 7.28−7.22 (m, 1H), 6.03−5.92 (m, 2H), 5.40−5.26 (m, 2H), 4.70 (d, 2H, J = 5.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 161.8, 149.8, 142.1, 134.0, 132.0, 131.9, 128.1, 118.5, 106.6, 95.2, 65.2. MS (ESI, + Ve) m/z (relative intensity) 380.95 ([M + Na]$^+$, 100%), 738.8 ([2M + Na]$^+$, 40%).

(E)-2-((Prop-2-ynyloxy)carbonyl)vinyl 2-Iodobenzoate[16] ***(1i)***. Following method A, compound **1i** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and prop-2-ynyl propiolate (239 mg, 2.21 mmol) as a colorless liquid (545 mg, 76% yield); IR 3088, 2925, 2851, 2135, 1753, 1718, 1658, 1573, 1435, 1374, 1272, 1245, 1131, 1103, 1007 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, 1H, J = 12.4 Hz), 8.09 (t, 1H, J = 7.6 Hz), 7.98 (dd, 1H, J_1 = 8 Hz, J_2 = 1.6 Hz), 7.52−7.45 (m, 1H), 7.28−7.23 (m, 1H), 5.95 (d, 1H, J = 12.4), 4.80 (d, 2H, J = 2.4 Hz), 2.53 (t, 1H, J = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 161.7, 150.5, 142.1, 134.1, 132.0, 131.7, 128.1, 105.9, 95.3, 77.4, 75.1, 52.1. MS (ESI, + Ve) m/z (relative intensity) 356.11 ([M + 1]$^+$, 100%).

(E)-3-Oxo-3-(p-tolyloxy)prop-1-en-1-yl 2-Iodobenzoate ***(1j)***. Following method A, compound **1j** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and *p*-tolyl propiolate (354 mg, 2.21 mmol) as a colorless liquid (535 mg, 65% yield); FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, 1H, J = 12.4 Hz), 8.11 (dd, 1H, J_1 = 8 Hz, J_2 = 0.8 Hz), 8.02 (dd, 1H, J_1 = 8 Hz, J_2 = 1.6 Hz), 7.55−7.47 (m, 1H), 7.32−7.24 (m 1H), 7.22 (d, 2H, J = 8.4 Hz), 7.09−7.02 (m, 2H), 6.11 (d, 1H, J = 12.4 Hz), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 161.7, 150.9, 148.1, 142.1, 135.6, 134.1, 132.0, 131.8, 130.0, 128.2, 121.2, 106.3, 95.3, 20.9. HRMS (ESI -TOF) m/z calcd for $C_{17}H_{14}IO_4$ [M + H]$^+$ 408.9937; Found 408.9929.

(E)-3-(2-Methoxyethoxy)-3-oxoprop-1-en-1-yl 2-Iodobenzoate[16] ***(1k)***. Following method A, compound **1k** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and 2-methoxyethyl propiolate (283 mg, 2.21 mmol) as a yellow solid (568 mg, 75% yield); mp 80 °C; FTIR 1429, 1464, 1506, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, 1H, J = 12.8 Hz), 8.10−8.04 (m, 1H), 7.99−7.92 (m, 1H), 7.51−7.43 (m, 1H), 7.28−7.20 (m, 1H), 5.95 (d, 1H, J = 12.8 Hz), 4.37−4.31 (m, 2H), 3.68−3.62 (m, 2H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 161.8, 149.9, 142.1, 134.0, 132.0, 131.8, 128.1, 106.5, 95.2, 70.4, 63.7, 59.0. MS ESI m/z 399 ([M + Na]$^+$, 100%).

(E)-3-(4-Methoxyphenyl)-3-oxoprop-1-en-1-yl 2-Iodobenzoate ***(1l)***. Following method A, compound **1l** was obtained from the reaction of 2-iodo benzoic acid (500 mg, 2.01 mmol) and 1-(4-methoxyphenyl)prop-2-yn-1-one (354 mg, 2.21 mmol) as a yellow solid (567 mg, 69% yield); mp 80 °C; FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, 1H, J = 12 Hz), 8.13−8.06 (m, 1H), 8.04−7.94 (m, 3H), 7.54−7.46 (m, 1H), 7.31−7.22 (m, 1H), 7.03−6.94 (m, 3H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.4, 163.6, 162.1, 149.7, 142.0, 134.0, 132.1, 131.9, 130.7, 130.6, 128.1, 113.9, 110.7, 95.2, 55.5. MS ESI (GC) m/z 407 [M]$^+$, 207 (100); HRMS (ESI-TOF) m/z calcd for $C_{17}H_{14}IO_4$ [M + H]$^+$ 408.9937; Found 408.9930.

(E)-3-Ethoxy-3-oxoprop-1-en-1-yl 2-Iodo-6-methylbenzoate ***(1m)***. Following method A, compound **1m** was obtained from the reaction of 2-iodo-6-methylbenzoic acid (500 mg, 1.91 mmol) and ethyl propiolate (206 mg, 2.10 mmol) as a yellow solid (563 mg, 82% yield): mp 80 °C; FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, 1H, J_1 = 12.4 Hz, J_2 = 1.6 Hz), 7.67−7.61 (m, 1H), 7.18 (d, 1H, J = 8 Hz), 7.06−6.98 (m, 1H), 5.85 (dd, 1H, J_1 = 12.4 Hz, J_2 = 1.6 Hz), 4.21 (q, 2H, J = 2 Hz), 2.31 (s, 3H), 1.28 (t, 3H, J = 2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.5, 149.3, 137.5, 137.3, 136.6, 131.6, 129.9, 107.5, 91.8, 60.6, 20.1, 14.2. MS ESI (GC) m/z 359 [M]$^+$, 207 (100). HRMS (ESI -TOF) m/z calcd for $C_{13}H_{14}IO_4$ [M + H]$^+$ 360.9937; Found 360.9991.

(E)-3-Ethoxy-3-oxoprop-1-en-1-yl 2,5-Diiodobenzoate ***(1n)***. Following method A, compound **1n** was obtained from the reaction of 2,5-diiodobenzoic acid (500 mg, 1.34 mmol) and ethyl propiolate (144 mg, 1.47 mmol) as a yellow solid (473 mg, 75% yield); mp 80 °C; FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, 1H, J = 12.4 Hz), 8.23 (s, 1H), 7.77 (d, 1H, J = 8.4 Hz), 7.57−7.51 (m, 1H), 5.95 (d, 1H, J = 12.4 Hz), 4.26 (q, 2H, J = 6.8 Hz), 1.33 (t, 3H, J = 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 160.6, 149.2, 143.3, 142.8, 140.4, 133.7, 107.5, 94.4, 93.1, 6.7, 14.2. HRMS (ESI -TOF) m/z calcd for $C_{12}H_{11}I_2O_4$ [M + H]$^+$ 472.8747; Found 472.8739.

(E)-4-Ethoxy-4-oxobut-2-en-2-yl 2-Iodobenzoate ***(1o)***. Following method B, compound **1o** was obtained from the reaction of 2-iodobenzoyl chloride (in situ prepared from 500 mg of acid) and ethyl acetoacetate (262 mg, 2.02 mmol) as a colorless oil (474 mg, 65% yield); FTIR 1430, 1465, 1507, 1583, 1653, 1729, 1755 cm^{-1}; ^{1}H

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NMR (400 MHz, $CDCl_3$) δ 8.09−8.03 (m, 1H), 7.90 (dd, 1H, J_1 = 7.6 Hz, J_2 = 1.6 Hz), 7.50−7.42 (m, 1H), 7.27−7.19 (m, 1H), 5.87 (s, 1H), 4.22 (q, 2H, J = 7.2 Hz), 2.51 (s, 3H), 1.31 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 165.7, 165.6, 141.7, 133.4, 131.5, 128.1, 110.7, 94.5, 60.3, 18.2, 14.2. HRMS (ESI -TOF) m/z calcd for $C_{13}H_{14}IO_4$ $[M + H]^+$ 360.9937; Found 360.9928.

*(E)-3-Ethoxy-3-oxo-1-phenylprop-1-en-1-yl 2-Iodobenzoate (**1p**).* Following method B, compound **1p** was obtained from the reaction of 2-iodobenzoyl chloride (in situ prepared from 500 mg of acid) and ethyl benzoylacetate (387 mg, 2.02 mmol) as a yellow solid (538 mg, 63% yield); mp 98 °C; FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, 1H, J = 8 Hz), 8.10 (d, 1H, J = 8 Hz), 7.68 (d, 2H, J = 8 Hz), 7.57−7.49 (m, 1H), 7.49−7.40 (m, 3H), 7.29−7.22(m, 1H), 6.40 (s, 1H), 4.19 (q, 2H, J = 7.2 Hz), 1.24 (t, 3H, J = 7.2 Hz);^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 162.9, 157.7, 141.7, 133.4, 133.2, 133.0, 132.3, 131.0, 128.8, 128.1, 126.1, 106.8, 95.2, 60.4, 14.1. HRMS (ESI -TOF) m/z calcd for $C_{18}H_{16}IO_4$ $[M + H]^+$ 423.0093; Found 423.0085.

*(E)-4-Oxopent-2-en-2-yl 2-Iodobenzoate (**1q**).* Following method B, compound **1q** was obtained from the reaction of 2-iodobenzoyl chloride (in situ prepared from 500 mg of acid) and acetylacetone (202 mg, 2.02 mmol) as a colorless oil in (407 mg, 61% yield); FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, 1H, J = 8 Hz), 7.93−7.87 (m, 1H), 7.51−7.43 (m, 1H), 7.27−7.19 (m, 1H), 6.27 (s, 1H), 2.47 (s, 1H), 2.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 162.5, 141.8, 133.5, 133.4, 131.5, 128.2, 128.1, 116.7, 94.6, 32.2, 18.6. MS ESI (GC) m/z 330 $[M]^+$, 231 (100); HRMS (ESI -TOF) m/z calcd for $C_{12}H_{12}IO_3$ $[M + H]^+$ 330.9831; Found 330.9823.

*(E)-3-Ethoxy-3-oxoprop-1-en-1-yl Benzoate[23] (**4a**).* Following method A, compound **4a** was obtained from the reaction of benzoic acid (500 mg, 4.09 mmol) and ethyl propiolate (441 mg, 4.50 mmol) as a colorless oil (766 mg, 85% yield); FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, 1H, J = 12.4 Hz), 8.12 (d, 2H, J = 8 Hz), 7.67−7.61 (m, 1H), 7.51 (t, 2H, J = 8 Hz), 5.91 (d, 1H, J = 12.4 Hz), 4.25 (q, 2H, J = 7.2 Hz), 1.32 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 162.5, 149.8, 134.4, 130.3, 128.7, 127.6, 106.4, 60.5, 14.2. MS ESI (GC) m/z 220 $[M]^+$, 105 (100).

*(E)-4-Ethoxy-4-oxobut-2-en-2-yl Benzoate[24] (**4b**).* Following method C, compound **4b** was obtained from the reaction of benzoyl chloride (500 mg, 3.57 mmol) and ethyl acetoacetate (463 mg, 3.56 mmol) as a colorless oil (624 mg, 75% yield); FTIR 1429, 1464, 1506, 1583, 1653, 1730, 1755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, 2H, J = 7.6 Hz), 7.65−7.57 (m, 1H), 7.47 (t, 2H, J = 7.6 Hz), 5.82 (s, 1H), 4.19 (q, 2H, J = 7.2 Hz), 2.48 (s, 3H), 1.28 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 164.1, 163.9, 133.8, 130.0, 128.8, 128.4, 110.4, 60.2, 18.2, 14.2. MS ESI (GC) m/z 234 $[M]^+$, 105 (100).

*4-Oxopent-2-en-2-yl Benzoate[24] (**4c**).* Following method C, compound **4c** was obtained from the reaction of benzoyl chloride (500 mg, 3.57 mmol) and acetylacetone (357 mg, 3.57 mmol) as a mixture (E:Z = 2:1) (530 mg, 73% yield); FTIR 1430, 1464, 1507, 1583, 1653, 1730, 1756 cm^{-1}; For E isomer: colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12−8.01 (m, 2H), 7.68−7.56 (m, 1H), 7.55−7.40 (m, 2H), 6.24 (s, 1H), 2.45 (s, 3H), 2.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 164.0, 162.9, 133.9, 130.0, 129.0, 128.6, 116.6, 32.2, 18.7. For Z isomer: colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ8.14−8.04 (m, 2H), 7.67−7.55 (m, 1H), 7.55−7.44 (m, 2H), 5.89 (s, 1H), 2.18 (s, 3H), 2.13 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 163.4, 158.2, 133.9, 130.1, 129.1, 128.3, 117.3, 31.0, 21.4. MS ESI (GC) m/z 204 $[M]^+$, 105 (100).

General Procedure for Preparation of Isocoumarin from 2-Iodo Enol Esters (1) (Method I). A mixture of enol ester **1** (50 mg), AgOAc (1 equiv), and dimethyl aminopyridine (DMAP) (1.2 equiv) in CH_3CN (2 mL) was stirred at room temperature for 12 h. Completion of the reaction was monitored by TLC. Then, the reaction mixture was charged for column chromatography over silica gel using a mixture of petroleum ether and ethyl acetate (9:1) as an eluent to enable the desired isocoumarin.

General Procedure for the Synthesis of Isocoumarin from 2-Iodo Benzoic Acid (3) at Room Temperature (Method II). A mixture of enol ester **4a** (50 mg), 2-iodobenzoic acid (1 equiv), AgOAc (1 equiv), and DMAP (2 equiv) in CH_3CN (2 mL) was stirred at room temperature for 12 h. Then, the reaction mixture was charged for column chromatography over silica gel using a mixture of petroleum ether and ethyl acetate (9:1) as an eluent to produce the desired isocoumarin.

General Procedure for the Synthesis of Isocoumarin from 2-Iodo Benzoic Acid (3) at 50 °C (Method III). A mixture of enol ester (**4b** or **4c**) (50 mg), 2-iodobenzoic acid (1 equiv), AgOAc (1 equiv), and DMAP (2 equiv) in CH_3CN (2 mL) was heated at 50 °C for 12 h. Then, the reaction mixture was charged for column chromatography over silica gel using a mixture of petroleum ether and ethyl acetate (9:1) as an eluent to afford the desired isocoumarin.

*Ethyl 1-Oxo-1H-isochromene-4-carboxylate (**2a**).* Following method **I**, compound **2a** was prepared from the Ag-mediated annulation of **1a** as a white solid (30 mg, 95% yield). Following method **II**, compound **2a** was also prepared from the reaction of 2-iodobenzoic acid (**3a**) and enol ester (**4a**) as a white solid (39 mg, 79% yield): mp 68 °C; FTIR 2940, 1744, 1728, 1492, 1483, 1468, 1442, 1418 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, 1H, J = 8.4 Hz), 8.35 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 8.22 (s, 1H), 7.80−7.89 (m, 1H), 7.57−7.65 (m, 1H), 4.41 (q, 2H, J = 7.2 Hz), 1.43 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 160.9, 152.4, 135.4, 133.6, 129.9, 129.0, 125.4, 120.4, 110.1, 61.2, 14.2. HRMS (ESI-TOF) m/z calcd for $C_{12}H_{11}O_4$ $[M + H]^+$ 219.0659; Found 219.0648.

*Propyl 1-Oxo-1H-isochromene-4-carboxylate (**2b**).* Following method **I**, compound **2b** was prepared from **1b** as a colorless liquid (21 mg, 65% yield): FTIR 2940, 1744, 1736, 1728, 1492, 1483, 1468, 1459 1442, 1418 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, 1H, J = 8.4 Hz), 8.34 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 8.21 (s, 1H), 7.79−7.87 (m, 1H), 7.56−7.64 (m, 1H), 4.30 (t, 2H, J = 6.6 Hz), 1.75−1.88 (m, 2H), 1.05 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 160.8, 152.4, 135.4, 133.6, 129.9, 129.0, 125.4, 120.4, 110.1, 66.8, 22.0, 10.5. HRMS (ESI-TOF) m/z calcd for $C_{13}H_{13}O_4$ $[M + H]^+$ 233.0816; Found 233.0806.

*Butyl 1-Oxo-1H-isochromene-4-carboxylate (**2c**).* Following method **I**, compound **2c** was prepared from **1c** as a white solid (25 mg, 76% yield): mp 57 °C; FTIR 2925, 1752, 1744, 1736, 1492, 1483, 1468, 1459, 1427, 1418 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, 1H, J = 8 Hz), 8.34 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 8.20 (s, 1H), 7.79−7.88 (m, 1H), 7.56−7.64 (m, 1H), 4.35 (t, 2H, J = 6.6 Hz), 1.71−1.82 (m, 2H), 1.43−1.53 (m, 2H), 1.00 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 160.9, 152.4, 135.4, 133.6, 129.9, 129.0, 125.4, 120.4, 110.1, 65.1, 30.6, 19.2, 13.7. HRMS (ESI-TOF) m/z calcd for $C_{14}H_{15}O_4$ $[M + H]^+$ 247.0972; Found 247.0962.

*Pentyl 1-Oxo-1H-isochromene-4-carboxylate (**2d**).* Following method **I**, compound **2d** was prepared from **1d** as a yellowish liquid (25 mg, 74% yield): FTIR 2925, 1744, 1728, 1492, 1483, 1459, 1427, 1428 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, 1H, J = 8 Hz), 8.34 (d, 1H, J = 8 Hz), 8.20 (s, 1H), 7.83 (t, 1H, J = 7.6 Hz), 7.59 (t, 1H, J = 7.6 Hz), 4.33 (t, 2H, J = 6.8 Hz), 1.71−1.82 (m, 2H), 1.38−1.45 (m, 4H), 0.91-.098 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 160.9, 152.4, 135.4, 133.6, 129.9, 129.0, 125.4, 120.4, 110.1, 65.4, 28.3, 28.1, 22.3, 14.0. HRMS (ESI-TOF) m/z calcd for $C_{15}H_{17}O_4$ $[M + H]^+$ 261.1129; Found 261.1120.

*Octyl 1-Oxo-1H-isochromene-4-carboxylate (**2e**).* Following method **I**, compound **2e** was prepared from **1e** as a colorless liquid (28 mg, 80% yield): FTIR 2950, 1744, 1728, 1492, 1468, 1442, 1427, 1418 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, J = 8 Hz), 8.35 (dd, 1H, J_1 = 7.8 Hz, J_2 = 1 Hz), 8.21 (s, 1H), 7.80−7.89 (m, 1H), 7.57−7.65 (m, 1H), 4.34 (t, 2H, J = 6.6 Hz), 1.73−1.84 (m, 2H), 1.24−1.48 (m, 10H), 0.86−0.94 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 160.9, 152.4, 135.4, 133.6, 129.9, 129.0, 125.4, 120.4, 110.2, 65.4, 31.7, 29.2, 29.1, 28.6, 26.0, 22.6, 14.1. HRMS (ESI-TOF) m/z calcd for $C_{18}H_{23}O_4$ $[M + H]^+$ 303.1598; Found 303.1592.

*Cyclohexyl 1-Oxo-1H-isochromene-4-carboxylate (**2f**).* Following method **I**, compound **2f** was prepared from **1f** as a colorless liquid (22 mg, 66% yield): FTIR 1744, 1736, 1728, 1492, 1483, 1468, 1442, 1418

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cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, J = 8 Hz), 8.35 (dd, 1H, J_1 = 7.6 Hz, J_2 = 1.2 Hz), 8.20 (s, 1H), 7.80−7.88 (m, 1H), 7.56−7.64 (m, 1H), 5.01−5.11 (m, 1H), 1.37−1.66 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 160.9, 152.2, 135.3, 133.7, 129.9, 128.9, 125.4, 120.4, 110.5, 73.7, 31.6, 25.3, 23.7. HRMS (ESI -TOF) m/z calcd for $C_{16}H_{17}O_4$ $[M + H]^+$ 273.1129; Found 273.1118.

*Benzyl 1-Oxo-1H-isochromene-4-carboxylate (**2g**).* Following method **I**, compound **2g** was prepared from **1g** as a white solid (18 mg, 53% yield): mp 76 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, 1H, J = 8 Hz), 8.34 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 8.25 (s, 1H), 7.79−7.88 (m, 1H), 7.56−7.64 (m, 1H), 7.37−7.49 (m, 5H), 5.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 160.7, 152.8, 135.4, 135.3, 133.5, 130.0, 129.0, 128.7, 128.7, 128.6, 128.4, 125.3, 120.4, 109.9, 66.9. HRMS (ESI-TOF) m/z calcd for $C_{17}H_{13}O_4$ $[M + H]^+$ 281.0816; Found 281.0808.

*Allyl 1-Oxo-1H-isochromene-4-carboxylate (**2h**).* Following method **I**, compound **2h** was prepared from **1h** as a white solid (19 mg, 60% yield): mp 59 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, 1H, J = 8.4 Hz), 8.35 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 8.26 (s, 1H), 7.80−7.88 (m, 1H), 7.57−7.65 (m, 1H), 5.97−6.11 (m, 1H), 5.39−5.44 (m, 1H), 5.35 (dd, 1H, J_1 = 10.4 Hz, J_2 = 1.2 Hz), 4.81−4.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 160.8, 152.7, 135.4, 133.5, 131.6, 130.0, 129.1, 125.3, 120.4, 119.1, 109.9, 65.8. HRMS (ESI -TOF) m/z calcd for $C_{13}H_{11}O_4$ $[M + H]^+$ 231.0659; Found 231.0649.

*Prop-2-yn-1-yl 1-Oxo-1H-isochromene-4-carboxylate (**2i**).* Following method **I**, compound **2i** was prepared from **1i** as a white solid (22 mg, 70% yield): mp 104 °C; FTIR 2323, 1744, 1728, 1647, 1492, 1451, 1427, 1408 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, J = 8.4 Hz), 8.35 (dd, 1H, J_1 = 8 Hz, J_2 = 1.2 Hz), 829 (s, 1H), 7.81−7.90 (m, 1H), 7.58−7.66 (m, 1H), 4.95 (d, 2H, J = 2.4 Hz), 2.58 (t, 1H, J = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 160.6, 153.2, 135.5, 133.2, 130.0, 129.2, 125.3, 120.3, 109.3, 77.1, 75.6, 52.5. HRMS (ESI -TOF) m/z calcd for $C_{13}H_9O_4$ $[M + H]^+$ 229.0503; Found 229.0494.

*p-Tolyl 1-Oxo-1H-isochromene-4-carboxylate (**2j**).* Following method **I**, compound **2j** was prepared from **1j** as a white solid (16 mg, 47% yield): mp 76 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, 1H, J = 8 Hz), 8.51 (S, 1H), 8.39 (dd, 1H, J_1 = 6.8 Hz, J_2 = 1.2 Hz), 7.82−7.90 (m, 1H), 7.60−7.68 (m, 1H), 7.27 (d, 2H, J = 8.4 Hz), 7.10 (dd, 2H, J_1 = 6.4 Hz, J_2 = 2 Hz), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 160.6, 153.6, 147.7, 136.1, 135.6, 133.3, 130.1, 130.0, 129.2, 125.4, 121.3, 120.3, 109.5, 20.9. HRMS (ESI -TOF) m/z calcd for $C_{17}H_{13}O_4$ $[M + H]^+$ 281.0184; Found 281.0180.

*2-Methoxyethyl 1-Oxo-1H-isochromene-4-carboxylate (**2k**).* Following method **I**, compound **2k** was prepared from **1k** as a white solid (23 mg, 71% yield): mp 58 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, 1H, J = 8.4 Hz), 8.35 (dd, 1H, J_1 = 8 Hz, J_2 = 2.8 Hz), 8.26 (s, 1H), 7.80−7.88 (m, 1H), 7.57−7.65 (m, 1H), 4.47−4.53 (m, 2H), 3.71−3.77 (m, 2H), 3.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0, 160.8, 152.7, 135.4, 133.5, 130.0, 129.0, 125.3, 120.3, 109.9, 70.3, 64.1, 59.0. HRMS (ESI-TOF) m/z calcd for $C_{13}H_{13}O_5$ $[M + H]^+$ 249.0765; found 249.0755.

*4-(4-Methoxybenzoyl)-1H-isochromen-1-one (**2l**).* Following method **I**, compound **2l** was prepared from **1l** as a white solid (25 mg, 72% yield): mp 76 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, 1H, J = 8 Hz), 8.0 (d, 1H, J = 8 Hz), 7.92 (dd, 2H, J_1 = 6.8 Hz, J_2 = 2 Hz), 7.76−7.84 (m, 1H), 7.59- 7.67 (m, 2H), 7.01 (dd, 2H, J_1 = 7 Hz, J_2 = 1.8 Hz), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.8, 164.2, 160.8, 149.7, 135.2, 134.3, 132.4, 130.3, 130.0, 129.3, 125.2, 120.9, 118.2, 114.0, 55.6. HRMS (ESI -TOF) m/z calcd for $C_{17}H_{13}O_4$ $[M + H]^+$ 281.0814; Found 281.0806.

*Ethyl 8-Methyl-1-oxo-1H-isochromene-4-carboxylate (**2m**).* Following method **I**, compound **2m** was prepared from **1m** as a colorless liquid (20 mg, 63% yield). Following method **II**, compound **2m** was also prepared from the reaction of **3d** and **4a** as a white solid (25 mg, 48% yield): FTIR 2925, 2877, 1744, 1728, 1492, 1483, 1468, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, 1H, J = 8.4 Hz), 8.16 (s, 1H), 7.67 (t, 1H, J = 7.8 Hz), 7.39 (d, 1H, J = 7.6 Hz), 4.39 (q, 2H, J = 7.2 Hz), 2.83 (s, 3H), 1.41 (t, 3H, J = 7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 160.0, 152.3, 143.8, 135.0, 134.5, 132.0, 123.2, 118.8, 110.2, 61.1, 23.8, 14.2; HRMS (ESI -TOF) m/z calcd for $C_{13}H_{13}O_4$ $[M + H]^+$ 233.0816; Found 233.0804.

*Ethyl 7-Iodo-1-oxo-1H-isochromene-4-carboxylate (**2n**).* Following method **I**, compound **2n** was prepared from the reaction of **1n** as a white solid (16 mg, 45% yield). Following method **II**, compound **2n** was also prepared from the reaction of **3b** and **4a** as a white solid (33 mg, 42% yield); mp 128 °C; FTIR 2910, 1752, 1736, 1728, 1483, 1459, 1435, 1418; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, 1H, J = 2 Hz), 8.45 (d, 1H, J = 8.8 Hz), 8.24 (s, 1H), 8.12 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2 Hz), 4.40 (q, 2H, J = 7.2 Hz), 1.41 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 159.3, 152.8, 144.1, 138.5, 132.8, 127.1, 121.8, 109.7, 94.0, 61.4, 14.2. HRMS (ESI -TOF) m/z calcd for $C_{12}H_{10}IO_4$ $[M + H]^+$ 344.9626; Found 344.9618.

*Ethyl 3-Methyl-1-oxo-1H-isochromene-4-carboxylate[25] (**2o**).* Following method **I**, compound **2o** was prepared from the reaction of **1o** as a yellowish liquid (25 mg, 78% yield). Following method **II**, compound **2o** was also prepared from the reaction of **3a** and **4b** as a yellowish liquid (32 mg, 65% yield): FTIR 2925, 1752, 1736, 1720, 1712, 1492, 1483, 1475, 1459, 1442 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, 1H, J_1 = 7.6 Hz, J_2 = 0.8 Hz), 7.70−7.81 (m, 2H), 7.48−7.56 (m, 1H), 4.46 (q, 2H, J = 7.2 Hz), 2.47 (s, 3H), 1.44 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.2, 157.6, 135.1, 134.6, 129.6, 128.1, 124.1, 119.4, 110.2, 61.7, 19.3, 14.2.

*Ethyl 1-Oxo-3-phenyl-1H-isochromene-4-carboxylate[25] (**2p**).* Following method **I**, compound **2p** was prepared from **1p** as a colorless liquid (18 mg, 51% yield): FTIR 2975, 1744, 1736, 1712, 1483, 1468, 1460, 1459, 1451, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, 1H, J_1 = 7.2 Hz, J_2 = 1.2 Hz), 8.03 (dd, 1H, J_1 = 8.8 Hz, J_2 = 1.8 Hz), 7.73−7.84 (m, 2H), 7.63−7.69 (m, 2H), 7.49 7.64 (m, 1H), 7.26−7.52 (m, 3H), 4.22 (q, 2H, J = 7.2 Hz), 1.06 (t, 3H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 161.1, 155.4, 135.3, 134.6, 132.6, 130.5, 129.9, 128.8, 128.4, 128.1, 124.1, 119.8, 110.9, 61.9, 13.56.

*4-Acetyl-3-methyl-1H-isochromen-1-one[26] (**2q**).* Following method **I**, compound **2q** was prepared from **1q** as a white solid (20 mg, 65% yield). Following method **III**, compound **2q** was also prepared from the reaction of **3a** and **4c** as a white solid (23 mg, 47% yield): mp 102 °C; FTIR 1752, 1736, 1696, 1492, 1459, 1442, 1427, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, 1H, J_1 = 7.6 Hz, J_2 = 1.0 Hz), 7.71−7.79 (m, 1H), 7.51−7.58 (m, 1H), 7.34 (d, 1H, J = 8 Hz), 2.60 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 161.3, 152.6, 135.1, 134.3, 130.1, 128.3, 123.0, 119.8, 118.5, 32.4, 18.3.

*Ethyl 7-Chloro-1-oxo-1H-isochromene-4-carboxylate (**5a**).* Following method **II**, compound **5a** was prepared from the reaction of **3c** and **4a** as a white solid (36 mg, 63% yield): mp 94 °C; FTIR 2925, 2901, 1736, 1720, 1712, 1483, 1468, 1451, 1435 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, 1H, J = 8.8 Hz), 8.28 (d, 1H, J = 2.4 Hz), 8.21 (s, 1H), 7.76 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.4 Hz), 4.40 (q, 2H, J = 7.2 Hz), 1.41 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 159.7, 152.5, 135.6, 135.0, 132.0, 129.3, 127.2, 121.7, 109.6, 61.4, 14.2. MS ESI (GC) m/z 252 $[M]^+$, 168 (100); HRMS (ESI -TOF) m/z calcd for $C_{12}H_{10}ClO_4$ $[M + H]^+$ 253.0268; Found 253.0258.

*Ethyl 7-Iodo-3-methyl-1-oxo-1H-isochromene-4-carboxylate (**5b**).* Following method **III**, compound **5b** was prepared from the reaction of **3b** and **4b** as a white solid (37 mg, 48% yield): mp 100 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, 1H, J = 2 Hz), 8.03 (dd, 1H, J_1 = 8.8 Hz, J_2 = 1.8 Hz), 7.58 (d, 1H, J = 8.4 Hz), 4.46 (q, 2H, J = 7.2 Hz), 2.47 (s, 3H), 1.44 (t, 3H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.6, 158.84, 143.7, 138.2, 133.9, 125.9, 120.9, 109.7, 92.6, 61.8, 19.6, 14.2. MS ESI (GC) m/z 358 $[M]^+$ (100); HRMS (ESI -TOF) m/z calcd for $C_{13}H_{12}IO_4$ $[M + H]^+$ 358.9780; found 358.9768.

*Ethyl 7-Chloro-3-methyl-1-oxo-1H-isochromene-4-carboxylate (**5c**).* Following method **III**, compound **5c** was prepared from the reaction of **3c** and **4b** as a white solid (31 mg, 55% yield): mp 98 °C; FTIR 2925, 1744, 1736, 1720, 1475, 1459, 1451, 1435, 1412, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, 1H, J = 2.4 Hz), 7.80 (d, 1H, J = 8.4 Hz), 7.69 (dd, 1H, J_1 = 9 Hz, J_2 = 2.2 Hz), 4.46 (q, 2H, J = 7.2 Hz), 2.49 (s, 3H), 1.44 (t, 3H, J = 7 Hz); ^{13}C NMR (100 MHz,

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$CDCl_3$) δ 165.4, 460.1, 158.5, 135.4, 134.1, 133.0, 129.0, 126.0, 120.7, 109.6, 61.9, 19.5, 14.2. MS ESI (GC) m/z 266 $[M]^+$, 220 (100); HRMS (ESI-TOF) m/z calcd for $C_{13}H_{12}ClO_4$ $[M + H]^+$ 267.0424; Found 267.0417.

*4-Acetyl-7-iodo-3-methyl-1H-isochromen-1-one (**5d**).* Following method **III**, compound **5d** was prepared from the reaction of **3b** and **4c** as a white solid (36 mg, 45% yield): mp 128 °C; FTIR-1752, 1736, 1720, 1696, 1492, 1483, 1459, 1427, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, 1H, J = 2 Hz), 8.02 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.0 Hz), 7.10 (d, 1H, J = 8.4 Hz), 2.58 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 159.7, 153.5, 143.8, 138.7, 133.5, 124.7, 121.2, 118.11, 92.7, 32.4, 18.6. MS ESI (GC) m/z 328 $[M]^+$ (100); HRMS (ESI-TOF) m/z calcd for $C_{12}H_{10}IO_3$ $[M + H]^+$ 328.9675; Found 328.9667.

*4-Acetyl-7-chloro-3-methyl-1H-isochromen-1-one (**5e**).* Following method **III**, compound **5e** was prepared from the reaction of **3c** and **4c** as a yellow solid (24 mg, 41% yield): mp 128 °C; FTIR 1736, 1720, 1696, 1492, 1483, 1459, 1427, 1418, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, 1H, J = 2.4 Hz), 7.68 (dd, 1H, J_1 = 8.8 Hz, J_2 = 2.4 Hz), 7.32 (d, 1H, J = 8.8 Hz), 2.59 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.6, 160.1, 153.2, 135.4, 134.3, 132.7, 129.5, 124.8, 121.1, 117.9, 32.4, 18.5. MS ESI (GC) m/z 236 $[M]^+$, 221 (100); HRMS (ESI-TOF) m/z calcd for $C_{12}H_{10}ClO_3$ $[M + H]^+$ 237.0318; Found 237.0309.

*4-Acetyl-3,8-dimethyl-1H-isochromen-1-one (**5f**).* Following method **III**, compound **5f** was prepared from the reaction of **3d** and **4c** as a white solid (26 mg, 49% yield): mp 102 °C; FTIR 2942, 1752, 1736, 1696, 1492, 1483, 1459, 1427, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (t, 1H, J = 7.8 Hz), 7.32 (d, 1H, J = 7.6 Hz), 7.10 (d, 1H, J = 8.0 Hz), 2.83 (s, 3H), 2.56 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 160.7, 151.7, 144.2, 135.8, 134.3, 131.2, 120.9, 118.8, 118.2, 32.4, 23.5, 18.0. MS ESI (GC) m/z 216 $[M]^+$, 201 (100); HRMS (ESI-TOF) m/z calcd for $C_{13}H_{13}O_3$ $[M + H]^+$ 217.0865; Found 217.0855.

*4-Acetyl-3-methyl-1-oxo-1H-isochromene-7-carbonitrile (**5g**).* Following method **III**, compound **5g** was prepared from the reaction of **3e** and **4c** as a white solid (22 mg, 40% yield): mp 172 °C; FTIR 2371, 1752, 1736, 1696, 1492, 1483, 1459, 1427, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, 1H, J = 1.6 Hz), 7.95 (dd, 1H, J_1 = 8.8 Hz, J_2 = 1.8 Hz), 7.49 (d, 1H, J = 8.4 Hz), 2.61 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 159.2, 156.3, 137.6, 137.3, 134.5, 124.3, 120.3, 117.8, 117.2, 112.1, 32.5, 18.9. MS ESI (GC) m/z 227 $[M]^+$, 212 (100); HRMS (ESI-TOF) m/z calcd for $C_{13}H_{10}NO_3$ $[M + H]$ 228.0661; Found 228.0656.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02602.

Copies of ^1H and ^{13}C NMR of enol esters and isocoumarins (PDF)

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Notes

The authors declare no competing financial interest.

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