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# Synthesis of Cyclohexane-Fused Isocoumarins via Cationic Palladium(II)-Catalyzed Cascade Cyclization Reaction of Alkyne-Tethered Carbonyl Compounds Initiated by Intramolecular Oxypalladation of Ester-Substituted Aryl Alkynes

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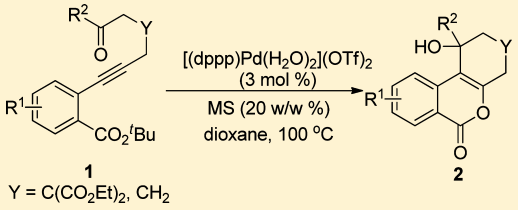
Supporting Information

**ABSTRACT:** A cationic Pd(II)-catalyzed cascade cyclization reaction of alkyne-tethered carbonyl compounds was developed. This reaction is initiated by intramolecular oxypalladation of alkynes with an ester group followed by 1,2-addition of the formed C−Pd(II) bond to the carbonyl group, providing a highly efficient method for the synthesis of cyclohexane-fused isocoumarins.




Transition metal-catalyzed cascade reactions have drawn considerable interest due to their high efficiency and diversity in constructing complex molecules.[1] Palladium-catalyzed cascade reactions, as essential tools for the formation of carbo- and heterocyclic compounds, have particularly experienced tremendous development based on fundamental mechanistic insight into elemental reactions.[2]

Isocoumarins not only extensively exist in natural products exhibiting a wide range of biological and pharmacological activities but also serve as important intermediates in the synthesis of a variety of heterocyclic compounds.[3] Traditional methods and transition metal-catalyzed reactions to approach this structure have been well-established.[4] However, palladium-catalyzed reactions are rarely reported in the synthesis of isocoumarins.[5] Recently, our group[5e] and Li[5f] reported palladium-catalyzed cascade reactions of 2-alkynylbenzoates with electron-deficient alkenes to deliver substituted isocoumarins conveniently (Scheme 1, eqs 1 and 2). These two reactions were initiated by oxypalladation of the alkyne with the intramolecular ester group and quenched by protonolysis and $\beta$-H elimination of the carbon−palladium bond.

In our previous work, a series of palladium(II)-catalyzed cascade reactions initiated by nucleopalladation of alkynes and quenched by 1,2-addition to a carbonyl or nitrile group to afford cyclic compounds have been successfully established.[6] Inspired by these works, palladium(II)-catalyzed intramolecular cascade cyclization of alkyne-tethered carbonyl compounds bearing an aryl ester to synthesize cycloalkane-fused isocoumarins was proposed (Scheme 1, eq 3). In the literature, only a few examples of an approach to such compounds have been reported.[5g,h]

Initially, the optimization of reaction conditions was carried out by using **1a** as the substrate under the catalysis of $Pd(OAc)_2$/bpy (Table 1, entry 1). A small amount of desired product **2a** was obtained with a moderate yield of inseparable byproduct **3a** (Table 1, entries 1 and 2). Without the catalyst and ligand, only **3a** was isolated in 53% yield in the presence of acetic acid (Table 1, entry 3). In the absence of acetic acid, the reaction was totally suppressed (Table 1, entry 4). From the above results, it can be seen that $Pd(OAc)_2$ was not effective enough for this cascade cyclization and that a highly active

**Scheme 1. Pd-Catalyzed Cascade Reactions of 2-Alkynylbenzoates**

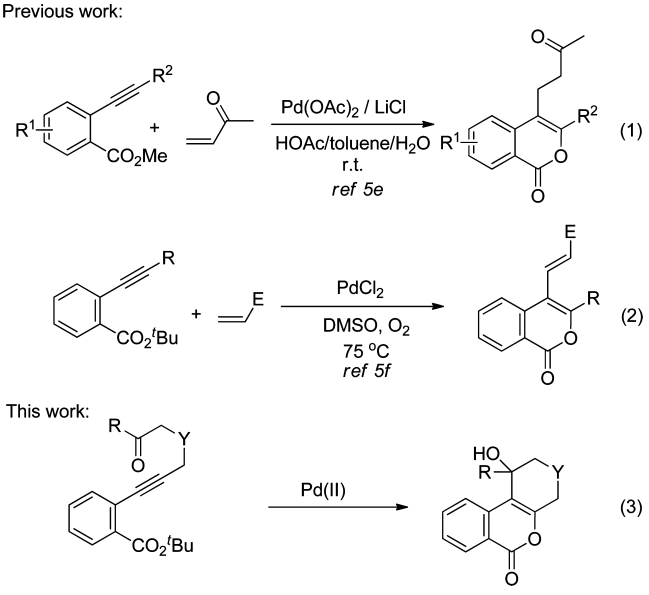



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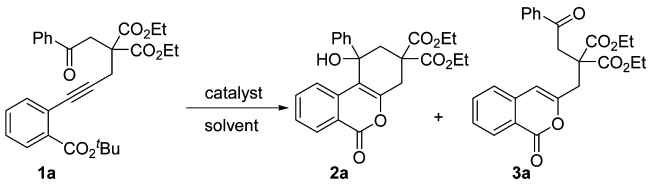
**Table 1. Optimization of the Reaction Conditions**[a]




| entry | catalyst (3 mol %) | solvent | temp (°C) | yield (%) (**2a**/**3a**)[b] |
|---|---|---|---|---|
| 1[c] | $Pd(OAc)_2$/bpy | HOAc/dioxane (1/4) | rt | 54 (~1/14) |
| 2[c] | $Pd(OAc)_2$/bpy | HOAc/dioxane (1/4) | 80 | 72 (~1/8) |
| 3 | | HOAc/dioxane (1/4) | 80 | 53 (**3a**) |
| 4[c] | $Pd(OAc)_2$/bpy | dioxane | 80 | no reaction |
| 5 | $[(bpy)Pd(H_2O)_2](OTf)_2$ | dioxane | 80 | 53 (~1/20) |
| 6[d] | $[(dppp)Pd(H_2O)_2](BF_4)_2$ | dioxane | 80 | 21 (~9/1) |
| 7 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | dioxane | 80 | 76 (~8/1) |
| 8 | $[(rac\text{-}binap)Pd(H_2O)_2](OTf)_2$ | dioxane | 80 | 45 (~1/6) |
| 9 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | MeCN | 80 | 81 (~1/1) |
| 10 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | DCE | 80 | 76 (~4/3) |
| 11 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | $C_6H_5CF_3$ | 80 | 88 (~1/2) |
| 12 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | THF | 80 | 89 (~4/1) |
| 13 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | DME | 80 | 66 (~2/1) |
| 14 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | DMF | 80 | Pd black |
| 15 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | dioxane | 60 | 89 (~2/1) |
| 16 | $[(dppp)Pd(H_2O)_2](OTf)_2$ | dioxane | 100 | 86 (~8/1) |
| 17[e] | $[(dppp)Pd(H_2O)_2](OTf)_2$ | dioxane | 100 | 78 (>20/1) |
| 18[e] | $[(dppp)Pd(H_2O)_2](OTf)_2$ | THF | 100 | 82 (~11/1) |
| 19[e] | $[(dppp)Pd(H_2O)_2](OTf)_2$ | DCE | 100 | 90 (~8/1) |

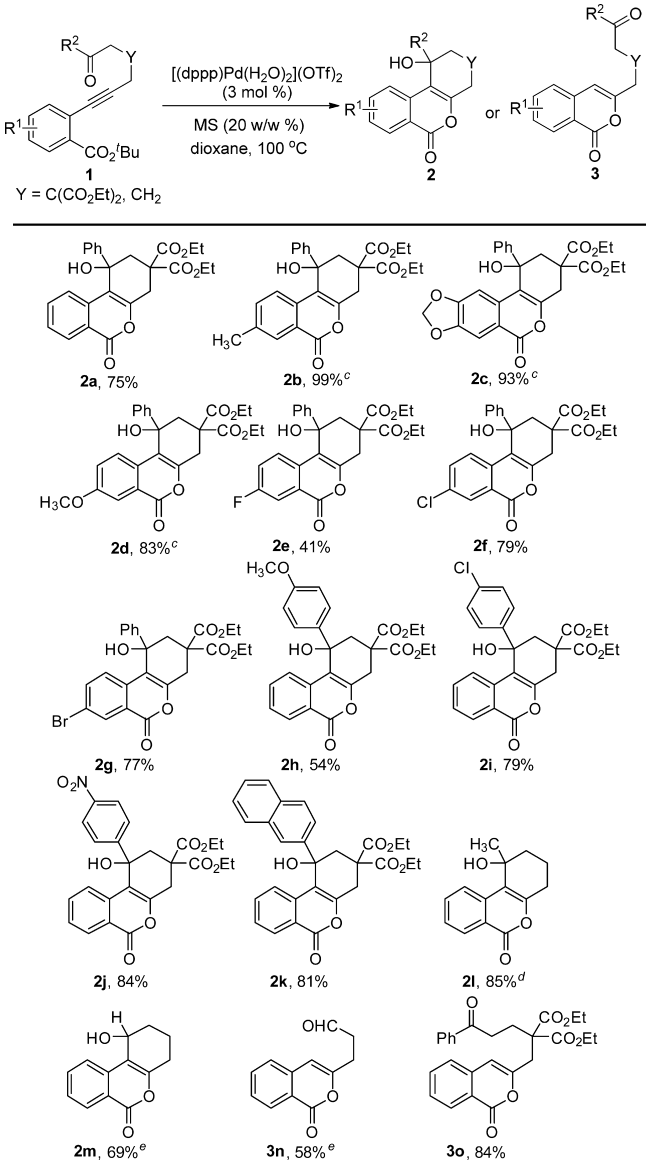
[a]Reaction conditions: **1a** (0.1 mmol, 1.0 equiv) and catalyst (3 mol %) were dissolved in solvents (1 mL) as shown in the table; the mixture was stirred at 80 °C until the consumption of **1a** as monitored by TLC. [b]Isolated yield; the ratio in the parentheses of product (**2a**/**3a**) was determined by $^1H$ NMR. [c]$Pd(OAc)_2$ (5 mol %) and bpy (6 mol %) were used. [d]Recovered 62% of **1a**. [e]Added MS of 4 Å (20 w/w %).

palladium catalyst might be needed. In our previous work, it was found that cationic palladium complexes had better catalytic activity than neutral ones, especially for the addition reactions to carbonyl groups.[7,8] Therefore, cationic palladium complexes were then tested.

The study revealed that $[(dppp)Pd(H_2O)_2](OTf)_2$ proved to be optimal to provide 76% total yield of the products (**2a**/**3a** = 8/1) (Table 1, entries 5–8) in dioxane. Subsequently, the effect of solvent and temperature were examined. Except DMF, moderate to good yields of the two products were obtained with different solvents, but the **2a**/**3a** ratio decreased significantly (Table 1, entries 9–14). Reducing or raising the temperature did not improve the reaction (Table 1, entries 15 and 16). Further investigation showed that the addition of MS of 4 Å effectively improved the yield of desired product **2a** by minimizing the formation of byproduct **3a** (Table 1, entry 17). The same effect could also be observed in THF or DCE for this new reaction; however, the result is not as good as with dioxane (Table 1, entries 18 and 19).

Having established the optimal conditions, our attention turned to an evaluation of the scope and limitations of this reaction. The results showed that substrates with an electron-donating group on the benzene ring gave good yields of cyclohexane-fused isocoumarins **2** and that only a very minor amount of the byproducts **3** were produced (Scheme 2, **2b**–**2d**). Substrates with bromo- or chloro- on the benzene ring can also give corresponding products in moderate yields, but the yield of fluorine-substituted product **2e** decreased dramatically

**Scheme 2. Substrate Scope of the Reaction**[a,b]




[a]Reaction conditions: **1** (0.2 mmol, 1.0 equiv), $[(dppp)Pd(H_2O)_2](OTf)_2$ (3 mol %) and MS of 4 Å (20%, w/w) were dissolved in dioxane (2 mL); the mixture was stirred at 100 °C until the consumption of **1** as monitored by TLC. [b]Isolated yield. [c]Trace amount of inseparable **3** was contained in the product. [d]Reaction performed at 80 °C. [e]Reaction performed at room temperature.



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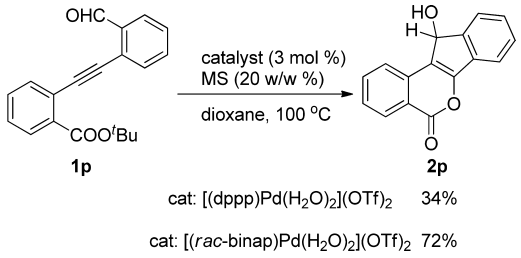
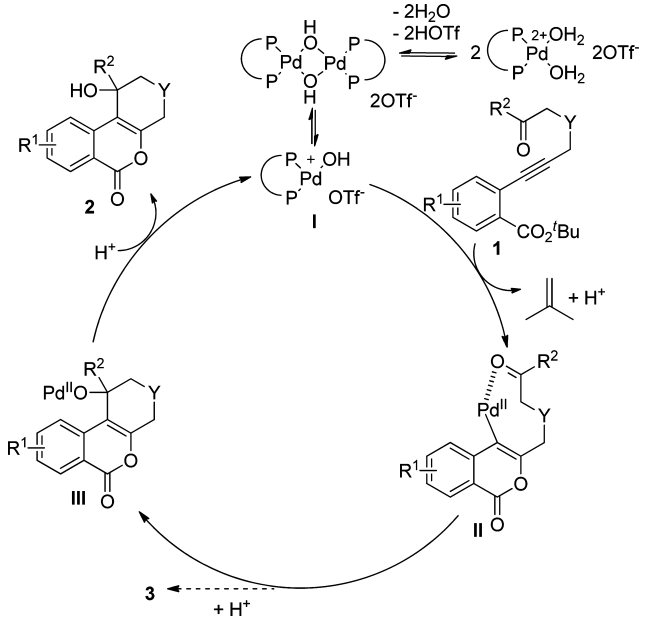
(Scheme 2, **2e**−**2g**). Then, the influence of different kinds of carbonyl groups was investigated. Compared to electron-donating group substituted aryl ketone **1h**, electron-withdrawing group substituted aryl ketone or 2-naphthyl ketone afforded a better result (Scheme 2, **2h**−**2k**). Alkyl ketones and aldehydes were also suitable for this cascade cyclization reaction under milder reaction conditions (Scheme 2, **2l** and **2m**). Unfortunately, when we attempted to synthesize the cyclopentane- or cycloheptane-fused isocoumarins using this procedure, the addition of the newly formed carbon−palladium bond to the carbonyl group did not occur at all, and only products **3n** and **3o** were observed. However, the reaction of phenyl-substituted substrate **1p** can proceed smoothly, leading to the double ring fused isocoumarin **2p** in 72% yield under the catalysis of $[(\text{rac-binap})Pd(H_2O)_2](OTf)_2$ (Scheme 3).

**Scheme 3. Reaction of Substrate 1p**




A proposed mechanism for the reaction is outlined in Scheme 4. First, the active cationic palladium(II) complex **I** was

**Scheme 4. Proposed Mechanism**




formed;[9] then, intramolecular oxypalladation of the ester group to alkyne with a loss of isobutene led to intermediate **II**.[10] When cationic palladium catalyst was used, a C−Pd bond added easily to intramolecular ketone followed by protonolysis to give product **2** and regenerated the active cationic palladium(II) species to complete the catalytic cycle. The ready protonolysis of the C−Pd bond of vinylpalladium species **II** in some cases to give product **3** in the reaction might be due to the electronic effect of the lone pair electrons on the oxygen atom, which increases the polarity of the C−Pd bond. In contrast to the neutral palladium species (e. g., $Pd(OAc)_2$), the success of the addition of the C−Pd bond to the ketone in most of our reactions might be due to the high Lewis acidity of cationic palladium catalyst, which can activate the carbonyl group.[7] As for similar reactions quenched by conjugate addition in eq 1, $Pd(OAc)_2$ can catalyze the process successfully instead, indicating that neutral palladium species may coordinate with the carbon−carbon double bond to undergo the subsequent addition.

In conclusion, we have accomplished a cationic palladium-catalyzed intramolecular cascade cyclization reaction of an alkyne-tethered carbonyl compound initiated by oxypalladation of the ester group with alkyne. This procedure provides a convenient and efficient method for the synthesis of cyclohexane-fused isocoumarins. A cationic palladium catalyst was the key for the success of this reaction.

## EXPERIMENTAL SECTION

**General Information.** All reactions were performed under nitrogen. All solvents were dried and distilled using standard procedures. Unless otherwise noted, reagents were obtained from commercial sources and used without further purification. $^1$H NMR and $^{13}$C NMR were recorded in deuterated chloroform ($CDCl_3$). Coupling constants are recorded in hertz, and chemical shifts are recorded as $\delta$ values in ppm. The following abbreviations are used to describe multiplicities: s = singlet, d = doublet, dd = double doublet, t = triplet, and m = multiplet. High-resolution mass spectra were carried out on a mass spectrometer with a TOF analyzer (ESI, EI). Infrared spectra were recorded on an FT-IR spectrometer. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. For column chromatography, silica gel of 200−300 mesh size was used.

**General Procedure for the Preparation of Substrates 1a−1l, 1o, and 1p.** A solution of *tert*-butyl 2-iodobenzoate[11] (2 mmol), terminal alkyne[12] (1.2 equiv), and $Pd(PPh_3)_2C1_2$ (70 mg, 0.05 equiv) in $Et_3N$ (10 mL) was stirred at room temperature for 5 min; then, CuI (19 mg, 0.05 equiv) was added, and the mixture was stirred at 70 °C overnight. After completion of the reaction as monitered by TLC, the suspension was filtered, and the filtrate was purified by silica gel column chromatography (ethyl acetate/petroleum ether, 1/12) to furnish the products.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1a**).* Yellow oil (701 mg, 71%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.08−8.06 (m, 2H), 7.80 (dd, $J$ = 7.8, 0.6 Hz, 1H), 7.56 (t, $J$ = 7.6 Hz, 1H), 7.45 (t, $J$ = 8.2 Hz, 2H), 7.40−7.33 (m, 2H), 7.31−7.27 (m, 1H), 4.25 (q, $J$ = 7.1 Hz, 4H), 4.10 (s, 2H), 3.41 (s, 2H), 1.51 (s, 9H), 1.25 (t, $J$ = 7.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.2, 169.4, 165.2, 136.5, 134.2, 133.6, 133.3, 130.9, 129.9, 128.5, 128.2, 127.5, 123.2, 89.8, 82.6, 81.2, 61.9, 55.1, 41.1, 28.0, 24.6, 13.9; IR (KBr) $\nu$ 2976, 2928, 2237, 1730, 1712, 1684, 1597, 1448, 1366, 1292, 1248, 1188, 1137, 1085, 1002, 848, 761, 688 cm$^{-1}$; MS ($m/z$, ESI) 510 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{29}H_{36}NO_7$ $[M + NH_4]^+$ 510.2486, found 510.2474.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)-4-methylphenyl)prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1b**).* Yellow solid (666 mg, 65%); mp 73−74 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (d, $J$ = 7.6 Hz, 2H), 7.59−7.54 (m, 2H), 7.45 (t, $J$ = 7.6 Hz, 2H), 7.28−7.25 (m, 1H), 7.15 (d, $J$ = 8.0 Hz, 1H), 4.24 (q, $J$ = 7.6 Hz, 4H), 4.08 (s, 2H), 3.38 (s, 2H), 2.34 (s, 3H), 1.50 (s, 9H), 1.24 (t, $J$ = 7.6 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.2, 169.5, 165.4, 137.7, 136.5, 134.2, 133.5, 133.3, 131.8, 130.4, 128.5, 128.2, 120.2, 88.7, 82.6, 81.2, 61.9, 55.1, 41.2, 28.1, 24.6, 21.2, 14.0; IR (KBr) $\nu$ 2972, 2928, 1732, 1712, 1683, 1597, 1449, 1358, 1300, 1258, 1183, 1160, 1081, 1046, 999, 850, 748, 687 cm$^{-1}$; MS ($m/z$, ESI) 524 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{30}H_{38}NO_7$ $[M + NH_4]^+$ 524.2643, found 524.2644.

*Diethyl 2-(3-(6-(tert-Butoxycarbonyl)benzo[d][1,3]dioxol-5-yl)-prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1c**).* Yellow oil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(924 mg, 87%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (d, $J$ = 7.2 Hz, 2H), 7.56 (t, $J$ = 7.4 Hz, 1H), 7.45 (t, $J$ = 7.6 Hz, 2H), 7.26 (s, 1H), 6.78 (s, 1H), 6.00 (s, 2H), 4.24 (q, $J$ = 7.2 Hz, 4H), 4.09 (s, 2H), 3.38 (s, 2H), 1.49 (s, 9H), 1.24 (t, $J$ = 7.0 Hz, 6H); $^{13}$C NMR (100 M, $CDCl_3$) $\delta$ 197.2, 169.4, 164.2, 149.7, 147.2, 136.5, 133.2, 128.5, 128.2, 128.1, 118.5, 113.4, 109.9, 102.0, 88.6, 82.5, 81.0, 61.9, 55.1, 41.1, 28.0, 24.6, 13.9; IR (KBr) $\nu$ 2979, 2931, 1736, 1719, 1687, 1600, 1504, 1370, 1249, 1183, 1124, 1034, 1002, 932, 857, 749, 689 cm$^{-1}$; MS ($m$/$z$, ESI) 554 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{30}H_{36}NO_9$ [M + $NH_4$]$^+$ 554.2385, found 554.2382.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)-4-methoxyphenyl)prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1d**).* Yellow oil (758 mg, 73%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (d, $J$ = 7.2 Hz, 2H), 7.56 (t, $J$ = 7.2 Hz, 1H), 7.45 (t, $J$ = 7.6 Hz, 2H), 7.32−7.28 (m, 2H), 6.90 (dd, $J$ = 2.8, 8.4 Hz, 1H), 4.25 (q, $J$ = 7.1 Hz, 4H), 4.09 (s, 2H), 3.80 (s, 3H), 3.39 (s, 2H), 1.50 (s, 9H), 1.25 (t, $J$ = 7.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 169.4, 165.0, 158.6, 136.4, 135.5, 134.9, 133.2, 128.4, 128.1, 117.1, 115.3, 114.7, 87.6, 82.3, 81.3, 61.8, 55.3, 55.0, 41.1, 27.9, 24.5, 13.9; IR (KBr) $\nu$ 2979, 2934, 2255, 1735, 1721, 1687, 1603, 1563, 1496, 1448, 1366, 1291, 1250, 1183, 1165, 1075, 1039, 1002, 911, 849, 730, 689 cm$^{-1}$; MS ($m$/$z$, ESI) 540 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{30}H_{38}NO_8$ [M + $NH_4$]$^+$ 540.2592, found 540.2592.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)-4-fluorophenyl)prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1e**).* Yellow oil (608 mg, 60%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (d, $J$ = 7.6 Hz, 2H), 7.57 (t, $J$ = 7.4, 1H), 7.51−7.43 (m, 3H), 7.36 (dd, $J$ = 4.8, 9.2 Hz, 1H), 7.06 (td, $J$ = 8.2, 2.4 Hz, 1H), 4.25 (q, $J$ = 7.1 Hz, 4H), 4.09 (s, 2H), 3.40 (s, 2H), 1.50 (s, 9H), 1.25 (t, $J$ = 7.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 169.4, 163.8 (d, $J_{CF}$ = 2.6 Hz), 161.3 (d, $J_{CF}$ = 248.8 Hz), 136.5, 136.0 (d, $J_{CF}$ = 7.8 Hz), 135.5 (d, $J_{CF}$ = 7.4 Hz), 133.3, 128.5, 128.2, 119.4 (d, $J_{CF}$ = 3.8 Hz), 118.4 (d, $J_{CF}$ = 21.9 Hz), 117.0 (d, $J_{CF}$ = 23.8 Hz), 89.6 (d, $J_{CF}$ = 1.8 Hz), 81.8, 81.5, 61.9, 55.0, 41.1, 27.9, 24.5, 13.9; IR (KBr) $\nu$ 2980, 2933, 2226, 1724, 1686, 1600, 1491, 1449, 1367, 1304, 1249, 1184, 1159, 1067, 1002, 942, 831, 749, 689 cm$^{-1}$; MS ($m$/$z$, ESI) 528 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{29}H_{35}FNO_7$ [M + $NH_4$]$^+$ 528.2392, found 528.2388.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)-4-chlorophenyl)prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1f**).* Yellow solid (281 mg, 27%); mp 59−60 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.06 (d, $J$ = 7.6 Hz, 2H), 7.76 (s, 1H), 7.57 (t, $J$ = 7.4 Hz, 1H), 7.45 (t, $J$ = 7.6 Hz, 2H), 7.31 (s, 2H), 4.25 (q, $J$ = 7.1 Hz, 4H), 4.08 (s, 2H), 3.41 (s, 2H), 1.50 (s, 9H), 1.24 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 169.3, 163.8, 136.5, 135.4, 135.0, 133.4, 133.3, 131.1, 130.0, 128.5, 128.2, 121.8, 91.1, 81.9, 81.6, 61.9, 55.0, 41.1, 28.0, 24.6, 14.0; IR (KBr) $\nu$ 2970, 2928, 1731, 1715, 1686, 1596, 1476, 1356, 1295, 1250, 1185, 1166, 1142, 1094, 1047, 999, 836, 746, 687 cm$^{-1}$; MS ($m$/$z$, ESI) 544 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{29}H_{35}ClNO_7$ [M + $NH_4$]$^+$ 544.2097, found 544.2095.

*Diethyl 2-(3-(4-Bromo-2-(tert-butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(2-oxo-2-phenylethyl)malonate (**1g**).* Yellow solid (910 mg, 82%); mp 62−63 °C; $^1$H NMR(400 MHz, $CDCl_3$) $\delta$ 8.06 (d, $J$ = 7.6 Hz, 2H), 7.92 (d, $J$ = 2.0 Hz, 1H), 7.57 (t, $J$ = 7.4 Hz, 1H), 7.48−7.43 (m, 3H), 7.24 (d, $J$ = 8.4 Hz, 1H), 4.24 (q, $J$ = 7.2 Hz, 4H), 4.09 (s, 2H), 3.40 (s, 2H), 1.50 (s, 9H), 1.24 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 169.3, 163.7, 136.4, 135.5, 135.1, 134.0, 133.3, 132.9, 128.5, 128.2, 122.2, 121.4, 91.3, 81.9, 81.7, 61.9, 55.0, 41.1, 28.0, 24.6, 13.9; IR (KBr) $\nu$ 2972, 2927, 2236, 1730, 1684, 1597, 1580, 1472, 1448, 1367, 1293, 1249, 1184, 1164, 1143, 1092, 1046, 999, 833, 760, 747, 688 cm$^{-1}$; MS ($m$/$z$, ESI) 588 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{29}H_{35}BrNO_7$ [M + $NH_4$]$^+$ 588.1591, found 588.1588.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(2-(4-methoxyphenyl)-2-oxoethyl)malonate (**1h**).* Yellow oil (810 mg, 78%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (d, $J$ = 9.2 Hz, 2H), 7.80 (dd, $J$ = 7.8, 0.6 Hz, 1H), 7.40−7.28 (m, 3H), 6.92 (d, $J$ = 8.8 Hz, 2H), 4.24 (q, $J$ = 6.8 Hz, 4H), 4.03 (s, 2H), 3.86 (s, 3H), 3.39 (s, 2H), 1.52 (s, 9H), 1.25 (t, $J$ = 7.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 195.6, 169.5, 165.2, 163.6, 134.3, 133.6, 130.9, 130.5, 129.9, 129.6, 127.5, 123.2, 113.6, 89.9, 82.5, 81.3, 61.9, 55.4, 55.1, 40.7, 28.0, 24.6, 13.9; IR (KBr) $\nu$ 2978, 2932, 1735, 1717, 1676, 1599, 1575, 1366, 1284, 1252, 1169, 1133, 1031, 832, 758 cm$^{-1}$; MS ($m$/$z$, ESI) 523 [M + H]$^+$; HRMS (ESI) calcd for $C_{30}H_{35}O_8$ [M + H]$^+$ 523.2326, found 523.2323.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(2-(4-chlorophenyl)-2-oxoethyl)malonate (**1i**).* Yellow oil (520 mg, 45%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.02 (d, $J$ = 8.4 Hz, 2H), 7.80 (d, $J$ = 8.0 Hz, 1H), 7.43−7.27 (m, 5H), 4.24 (q, $J$ = 6.9 Hz, 4H), 4.08 (s, 2H), 3.39 (s, 2H), 1.51 (s, 9H), 1.25 (t, $J$ = 7.0, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 196.1, 169.3, 165.1, 139.7, 134.9, 134.2, 133.6, 131.0, 130.0, 129.7, 128.8, 127.5, 123.2, 89.7, 82.6, 81.2, 62.0, 55.1, 41.1, 28.0, 24.6, 14.0; IR (KBr) $\nu$ 3475, 3377, 2978, 2925, 2221, 1732, 1686, 1591, 1448, 1365, 1286, 1249, 1183, 1136, 1085, 1067, 1047, 999, 861, 758, 692 cm$^{-1}$; MS ($m$/$z$, ESI) 544 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{29}H_{35}ClNO_7$ [M + $NH_4$]$^+$ 544.2097, found 544.2094.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(2-(4-nitrophenyl)-2-oxoethyl)malonate (**1j**).* Yellow solid (512 mg, 48%); mp 101−102 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.31−8.25 (m, 4H), 7.81 (dd, $J$ = 8.2, 1.0 Hz, 1H), 7.42−7.35 (m, 2H), 7.30 (td, $J$ = 7.5, 1.7 Hz, 1H), 4.29−4.23 (m, 4H), 4.18 (s, 2H), 3.40 (s, 2H), 1.52 (s, 9H), 1.26 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 196.1, 169.2, 165.0, 150.4, 141.0, 134.2, 133.6, 131.1, 130.0, 129.4, 127.6, 123.7, 123.1, 89.5, 82.8, 81.2, 62.1, 55.2, 41.7, 28.0, 24.7, 14.0; IR (KBr) $\nu$ 2977, 2914, 1733, 1709, 1691, 1602, 1529, 1446, 1345, 1285, 1250, 1184, 1138, 1085, 1069, 1004, 892, 781, 700 cm$^{-1}$; MS ($m$/$z$, ESI) 555 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{29}H_{35}N_2O_9$ [M + $NH_4$]$^+$ 555.2337, found 555.2334.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(2-(naphthalen-2-yl)-2-oxoethyl)malonate (**1k**).* Yellow oil (659 mg, 62%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.63 (s, 1H), 8.08 (dd, $J$ = 8.8, 1.6 Hz, 1H), 7.93 (d, $J$ = 8.0 Hz, 1H), 7.89−7.84 (m, 2H), 7.78 (dd, $J$ = 7.8, 1.4 Hz, 1H), 7.61−7.50 (m, 2H), 7.38 (dd, $J$ = 7.8, 1.0 Hz, 1H), 7.34−7.24 (m, 2H), 4.28 (q, $J$ = 7.1 Hz, 4H), 4.23 (s, 2H), 3.46 (s, 2H), 1.45 (s, 9H), 1.26 (t, $J$ = 7.0 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 197.1, 169.5, 165.2, 135.7, 134.2, 133.9, 133.7, 132.4, 130.9, 130.2, 129.9, 129.6, 128.5, 128.3, 127.7, 127.5, 126.6, 123.7, 123.1, 89.8, 82.6, 81.2, 62.0, 55.2, 41.1, 28.0, 24.6, 14.0; IR (KBr) $\nu$ 3061, 2978, 2931, 2238, 1735, 1718, 1680, 1469, 1366, 1281, 1255, 1180, 1132, 1083, 856, 818, 756 cm$^{-1}$; MS ($m$/$z$, ESI) 560 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{33}H_{38}NO_7$ [M + $NH_4$]$^+$ 560.2643, found 560.2641.

*tert-Butyl 2-(6-Oxohept-1-yn-1-yl)benzoate (**1l**).* Yellow oil (378 mg, 66%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.80 (d, $J$ = 7.2 Hz, 1H), 7.48−7.45 (m, 1H), 7.38 (t, $J$ = 7.4 Hz, 1H), 7.32−7.27 (m, 1H), 2.72 (t, $J$ = 7.4 Hz, 2H), 2.52 (t, $J$ = 6.8 Hz, 2H), 2.18 (s, 3H), 1.93−1.85 (m, 2H), 1.60 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 208.6, 165.8, 134.0, 133.9, 130.8, 129.8, 127.2, 123.5, 94.0, 81.3, 80.2, 42.1, 30.0, 28.1, 22.4, 19.0; IR (KBr) $\nu$ 3413, 3065, 2977, 2932, 2234, 1710, 1596, 1567, 1445, 1367, 1252, 1183, 1171, 1131, 1082, 1038, 954, 847, 757, 699 cm$^{-1}$; MS ($m$/$z$, ESI) 304 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{18}H_{26}NO_3$ [M + $NH_4$]$^+$ 304.1907, found 304.1909.

*Diethyl 2-(3-(2-(tert-Butoxycarbonyl)phenyl)prop-2-yn-1-yl)-2-(3-oxo-3-phenylpropyl)malonate (**1o**).* Yellow oil (617 mg, 52%); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.98−7.96 (m, 2H), 7.82 (dd, $J$ = 7.8, 1.0 Hz, 1H), 7.54−7.50 (m, 1H), 7.45−7.34 (m, 4H), 7.31 (dd, $J$ = 7.4, 1.4 Hz, 1H), 4.28−4.19 (m, 4H), 3.19 (s, 2H), 3.14 (t, $J$ = 8.0 Hz, 2H), 2.61 (t, $J$ = 8.0 Hz, 2H), 1.54 (s, 9H), 1.25 (t, $J$ = 7.2 Hz, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 198.7, 170.1, 165.2, 136.6, 134.5, 133.6, 132.9, 131.0, 129.9, 128.5, 128.0, 127.5, 123.1, 89.0, 82.7, 81.3, 61.7, 56.5, 33.8, 28.1, 27.2, 24.9, 14.0; IR (KBr) $\nu$ 3064, 2980, 2934, 2230, 1727, 1687, 1597, 1481, 1447, 1368, 1299, 1253, 1132, 1080, 1039, 849, 758, 692 cm$^{-1}$; MS ($m$/$z$, ESI) 524 [M + $NH_4$]$^+$; HRMS (ESI) calcd for $C_{30}H_{38}NO_7$ [M + $NH_4$]$^+$ 524.2643, found 524.2641.

*tert-Butyl 2-((2-Formylphenyl)ethynyl)benzoate (**1p**).* Yellow solid (581 mg, 95%); mp 66−67 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 10.75 (s, 1H), 7.96 (d, $J$ = 7.6 Hz, 1H), 7.92 (d, $J$ = 7.6 Hz, 1H), 7.67 (t, $J$ = 8.0 Hz, 2H), 7.59 (t, $J$ = 7.4 Hz, 1H), 7.51−7.39 (m, 3H), 1.60 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 192.4, 165.1, 136.1, 134.0, 133.8, 133.6, 133.1, 131.2, 130.2, 128.6, 128.5, 127.0, 126.9, 122.3, 95.0, 89.3, 81.7, 28.1; IR (KBr) $\nu$ 3066, 2979, 2930, 1712, 1688, 1590,



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1485, 1365, 1297, 1277, 1254, 1163, 1090, 877, 758, 698, 637 $cm^{-1}$; MS (*m*/*z*, ESI) 324 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{20}H_{22}NO_3$ $[M + NH_4]^+$ 324.1594, found 324.1594.

**General Procedure for the Preparation of Substrates 1m and 1n.** A solution of *tert*-butyl 2-iodobenzoate (1.5 g, 1 equiv), alkyn-1-ol (5 mmol, 1 equiv), and $Pd(PPh_3)_4$ (56 mg, 0.01 equiv) in $Et_3N$ (25 mL) was stirred at room temperature for 5 min; then, CuI (20 mg, 0.02 equiv) was added. The mixture was stirred at room temperature overnight. The suspension was filtered, and the filtrate was concentrated and oxidized with PCC (1.2 equiv) and Celite in DCM (20 mL). The suspension was filtered, and the filtrate was purified by silica gel column chromatography (ethyl acetate/petroleum ether, 1/12) to furnish the products.

*tert-Butyl 2-(6-Oxohex-1-yn-1-yl)benzoate (**1m**).* Yellow oil (1.04 g, 78%); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 9.84 (s, 1H), 7.81−7.79 (m, 1H), 7.47 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.38 (td, *J* = 7.6, 1.5 Hz, 1H), 7.32−7.28 (m, 1H), 2.72 (dd, *J* = 7.2, 1.2 Hz, 2H), 2.55 (t, *J* = 6.8 Hz, 2H), 1.99−1.92 (m, 2H), 1.60 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 202.0, 165.7, 134.0, 133.9, 130.8, 129.7, 127.3, 123.4, 93.5, 81.3, 80.4, 42.7, 28.1, 21.0, 19.1; IR (KBr) $\nu$ 2978, 2934, 2254, 1704, 1596, 1481, 1447, 1368, 1306, 1253, 1170, 1133, 1083, 910, 846, 758, 730, 648 $cm^{-1}$; MS (70 eV, EI) *m*/*z* (%) 246, 230, 214, 186, 173, 172, 160, 149, 115, 105, 76, 57; HRMS (EI) calcd for $C_{13}H_{11}O_3$ $[M\text{-}C_4H_9]^+$ 215.0708, found 215.0713.

*tert-Butyl 2-(5-Oxopent-1-yn-1-yl)benzoate (**1n**).* Yellow oil (701 mg, 55%); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 9.87 (s, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.38 (td, *J* = 7.6, 1.1 Hz, 1H), 7.32−7.28 (m, 1H), 2.79 (s, 4H), 1.60 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 200.6, 165.7, 134.0, 133.9, 130.8, 129.8, 127.4, 123.1, 92.4, 81.4, 80.3, 42.4, 28.1, 13.0; IR (KBr) $\nu$ 2978, 2932, 2725, 2233, 1786, 1706, 1597, 1481, 1445, 1367, 1304, 1253, 1170, 1130, 1082, 1040, 908, 846, 757 $cm^{-1}$; MS (*m*/*z*, ESI) 276 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{16}H_{22}NO_3$ $[M + NH_4]^+$ 276.1594, found 276.1591.

**General Procedure of the Cationic Palladium(II)-Catalyzed Cascade Cyclization Reaction of Alkyne-Tethered Carbonyl Compounds.** A suspension of $[(dppp)Pd(H_2O)_2](OTf)_2$ (5.3 mg, 3 mol %) and MS of 4 Å (20 w/w %) in dioxane (2 mL) was stirred at room temperature for 5 min under $N_2$; then, substrate **1** (0.2 mmol, 1 equiv) was added and stirred at 100 °C. After completion, the reaction mixture was purified by flash chromatography, eluting with ethyl acetate and petroleum ether (1/7) to afford the products. Compounds **2i**−**2k** and **2o** can be isolated from **3i**−**3k** and **3o** by the above chromatography. Compounds **2a**−**2d**, **2f**−**2h**, **2l**, **2m**, and **2p** cannot be separated from byproducts **3a**−**3d**, **3f**−**3h**, **3l**, **3m**, and **3p** by this method, and mixtures were obtained. Suspending the above mixture of **2** and **3** in petroleum ether (PE) and then filtering can give pure products **2a**−**2d**, **2f**−**2h**, **2l**, **2m**, and **2p** eventually (products **3** can dissolve in PE but **2** cannot). Product **2e** was isolated by chromatography again using PE/benzene/$Et_3N$ (20/5/2) as the eluent.

*Diethyl 1-Hydroxy-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2a**).* Yellow solid (67 mg, 75%); mp 139−140 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.25 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.43−7.28 (m, 7H), 7.22 (t, *J* = 7.2 Hz, 1H), 5.24 (s, 1H), 4.35−4.10 (m, 4H), 3.39 (d, *J* = 18.0 Hz, 1H), 3.30 (dd, *J* = 18.0, 2.4 Hz, 1H), 2.95 (dd, *J* = 15.2, 2.0 Hz, 1H), 2.24 (d, *J* = 14.8 Hz, 1H), 1.29−1.22 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.6, 169.4, 161.9, 150.2, 147.2, 135.3, 133.9, 129.5, 128.6, 127.5, 127.2, 126.9, 125.0, 121.6, 114.4, 73.2, 62.8, 62.3, 53.1, 47.6, 33.6, 13.9, 13.8; IR (KBr) $\nu$ 3488, 2995, 2923, 2852, 1743, 1713, 1641, 1487, 1448, 1370, 1272, 1244, 1218, 1186, 1163, 1091, 1073, 1033, 999, 865, 771, 696 $cm^{-1}$; MS (*m*/*z*, ESI) 437 $[M + H]^+$; HRMS (ESI) calcd for $C_{25}H_{25}O_7$ $[M + H]^+$ 437.1595, found 437.1592.

*Diethyl 2-((1-Oxo-1H-isochromen-3-yl)methyl))-2-(2-oxo-2-phenylethyl)malonate (**3a**).* Yellow oil; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.20 (d, *J* = 8.4 Hz, 1H), 7.98−7.95 (m, 2H), 7.63 (td, *J* = 7.6, 1.2 Hz, 1H), 7.60−7.55 (m, 1H), 7.45 (t, *J* = 7.6 Hz, 3H), 7.22 (d, *J* = 7.6 Hz, 1H), 6.19 (s, 1H), 4.33−4.24 (m, 4H), 3.81 (s, 2H), 3.48 (s, 2H), 1.28 (t, *J* = 7.2 Hz, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 197.0, 169.5, 161.7, 153.4, 136.6, 136.3, 134.7, 133.5, 129.4, 128.6, 128.1, 128.0, 125.2, 120.3, 106.4, 62.1, 54.7, 40.8, 36.6, 13.9; IR (KBr) $\nu$ 2982, 2934, 1728, 1685, 1657, 1599, 1448, 1357, 1283, 1184, 1041, 1021, 914, 858, 754, 730, 688 $cm^{-1}$; MS (*m*/*z*, ESI) 454 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{25}H_{28}NO_7$ $[M + NH_4]^+$ 454.1860, found 454.1865.

*Diethyl 1-Hydroxy-8-methyl-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2b**).* White solid (90 mg, 99%); mp 195−196 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.04 (s, 1H), 7.42 (br s, 2H), 7.31−7.27 (m, 3H), 7.23−7.18 (m, 2H), 5.17 (s, 1H), 4.34−4.07 (m, 4H), 3.38 (d, *J* = 17.6 Hz, 1H), 3.28 (dd, *J* = 18.0, 2.0 Hz, 1H), 2.94 (dd, *J* = 14.8, 2.4 Hz, 1H), 2.33 (s, 3H), 2.25 (d, *J* = 15.2 Hz, 1H), 1.28−1.22 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.4, 162.0, 149.3, 147.2, 137.6, 135.2, 132.7, 129.1, 128.5, 127.0, 126.8, 125.0, 121.4, 114.3, 73.1, 62.7, 62.2, 53.0, 47.5, 33.5, 21.0, 13.8, 13.7; IR (KBr) $\nu$ 3479, 2982, 1750, 1724, 1643, 1502, 1446, 1368, 1266, 1244, 1200, 1161, 1091, 1074, 1050, 997, 869, 832, 768, 707 $cm^{-1}$; MS (*m*/*z*, ESI) 451 $[M + H]^+$; HRMS (ESI) calcd for $C_{26}H_{27}O_7$ $[M + H]^+$ 451.1751, found 451.1759.

*Diethyl 1-Hydroxy-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-[1,3]-dioxolo[4′,5′4,5]benzo[1,2-c]chromene-3,3-dicarboxylate (**2c**).* White solid (89 mg, 93%); mp 193−194 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.55 (s, 1H), 7.40 (br s, 2H), 7.31−7.28 (m, 2H), 7.24−7.20 (m, 1H), 6.90 (s, 1H), 5.92 (dd, *J* = 11.8, 1.0 Hz, 2H), 5.29 (s, 1H), 4.34−4.06 (m, 4H), 3.37 (d, *J* = 18.0 Hz, 1H), 3.26 (dd, *J* = 18.0, 2.0 Hz, 1H), 2.93 (dd, *J* = 15.2, 2.4 Hz, 1H), 2.23 (d, *J* = 15.2 Hz, 1H), 1.28−1.21 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.3, 161.4, 152.8, 149.2, 147.4, 146.8, 133.1, 128.5, 127.1, 124.9, 116.2, 114.2, 107.0, 106.1, 101.9, 73.1, 62.8, 62.2, 52.9, 47.6, 33.4, 13.8, 13.7; IR (KBr) $\nu$ 3413, 3059, 2982, 2918, 1729, 1704, 1650, 1623, 1478, 1448, 1410, 1368, 1306, 1246, 1201, 1184, 1166, 1075, 1055, 1033, 1004, 912, 862, 830, 768, 702 $cm^{-1}$; MS (*m*/*z*, ESI) 481 $[M + H]^+$; HRMS (ESI) calcd for $C_{26}H_{25}O_9$ $[M + H]^+$ 481.1493, found 481.1499.

*Diethyl 1-Hydroxy-8-methoxy-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2d**).* White solid (75 mg, 83%); mp 143−144 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.64 (d, *J* = 2.8 Hz, 1H), 7.46−7.34 (m, 3H), 7.30−7.26 (m, 2H), 7.23−7.19 (m, 1H), 6.95 (dd, *J* = 9.0, 2.6 Hz, 1H), 5.22 (s, 1H), 4.34−4.07 (m, 4H), 3.80 (s, 3H), 3.38 (d, *J* = 17.6 Hz, 1H), 3.28 (dd, *J* = 17.6, 2.0 Hz, 1H), 2.94 (dd, *J* = 14.8, 2.0 Hz, 1H), 2.25 (d, *J* = 14.8 Hz, 1H), 1.28−1.21 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.4, 162.0, 158.6, 148.0, 147.1, 128.9, 128.5, 128.4, 127.1, 125.0, 123.3, 122.8, 114.2, 109.9, 73.1, 62.7, 62.2, 55.4, 53.0, 47.5, 33.3, 13.8, 13.7; IR (KBr) $\nu$ 3455, 2958, 2919, 2850, 1725, 1698, 1643, 1496, 1445, 1357, 1327, 1311, 1285, 1242, 1204, 1180, 1085, 1071, 1045, 1022, 1006, 896, 846, 788, 765, 701 $cm^{-1}$; MS (*m*/*z*, ESI) 467 $[M + H]^+$; HRMS (ESI) calcd for $C_{26}H_{27}O_8$ $[M + H]^+$ 467.1700, found 467.1692.

*Diethyl 8-Fluoro-1-hydroxy-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2e**).* White solid (36 mg, 41%); mp 151−152 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.88 (dd, *J* = 8.2, 2.8 Hz, 1H), 7.47 (dd, *J* = 9.0, 5.4 Hz, 1H), 7.40 (br s, 2H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.10 (td, *J* = 8.6, 2.8 Hz, 1H), 5.36 (s, 1H), 4.36−4.09 (m, 4H), 3.40 (d, *J* = 18.0 Hz, 1H), 3.28 (dd, *J* = 17.6, 2.6 Hz, 1H), 2.95 (dd, *J* = 15.2, 2.4 Hz, 1H), 2.24 (d, *J* = 15.2 Hz, 1H), 1.29−1.22 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.7, 169.3, 161.2 (d, $J_{CF}$ = 248.6 Hz), 161.0 (d, $J_{CF}$ = 3.4 Hz), 154.5, 149.4 (d, $J_{CF}$ = 2.3 Hz), 146.9, 131.9 (d, $J_{CF}$ = 2.7 Hz), 129.7 (d, $J_{CF}$ = 7.5 Hz), 128.7, 127.3, 125.0, 123.4 (d, $J_{CF}$ = 8.0 Hz), 122.2 (d, $J_{CF}$ = 22.4 Hz), 114.8 (d, $J_{CF}$ = 22.7 Hz), 114.1 (d, $J_{CF}$ = 1.1 Hz), 63.0, 62.4, 53.1, 47.5, 33.5, 13.9, 13.8; IR (KBr) $\nu$ 3478, 3070, 2983, 2923, 1749, 1723, 1648, 1494, 1447, 1368, 1306, 1263, 1240, 1203, 1166, 1093, 1067, 1000, 901, 875, 834, 767, 701 $cm^{-1}$; MS (*m*/*z*, ESI) 472 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{25}H_{27}FNO_7$ $[M + NH_4]^+$ 472.1766, found 472.1767.

*Diethyl 8-Chloro-1-hydroxy-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2f**).* White solid (75 mg, 79%); mp 201−202 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.19 (d, *J* = 2.4 Hz, 1H), 7.42−7.21 (m, 7H), 5.33 (s, 1H), 4.36−4.08 (m, 4H), 3.40 (d, *J* = 18.0 Hz, 1H), 3.28 (dd, *J* = 18.0, 1.6 Hz, 1H), 2.95 (dd, *J* = 15.2, 2.0 Hz, 1H), 2.25 (d, *J* = 15.2 Hz, 1H), 1.29−1.22 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.2, 160.7, 150.3, 146.8, 134.2,



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133.8, 133.4, 128.7, 128.6, 127.3, 124.9, 122.9, 114.1, 73.0, 62.9, 62.4, 53.0, 47.4, 33.5, 13.9, 13.7; IR (KBr) $\nu$ 3485, 2989, 1749, 1722, 1644, 1480, 1445, 1369, 1338, 1265, 1230, 1218, 1162, 1095, 1073, 1050, 900, 882, 861, 830, 768, 705 $cm^{-1}$; MS ($m/z$, ESI) 488 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{25}H_{27}ClNO_7$ $[M + NH_4]^+$ 488.1471, found 488.1487.

*Diethyl 8-Bromo-1-hydroxy-6-oxo-1-phenyl-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2g**).* White solid (79 mg, 77%); mp 217−218 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.35 (d, $J$ = 1.6 Hz, 1H), 7.47−7.27 (m, 6H), 7.24−7.21 (m, 1H), 5.33 (s, 1H), 4.34−4.10 (m, 4H), 3.38 (d, $J$ = 18.0 Hz, 1H), 3.27 (dd, $J$ = 18.0, 2.0 Hz, 1H), 2.94 (dd, $J$ = 15.2, 1.6 Hz, 1H), 2.24 (d, $J$ = 15.2 Hz, 1H), 1.29−1.22 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.6, 169.2, 160.6, 150.5, 146.8, 137.0, 134.1, 131.8, 128.8, 128.6, 127.3, 124.9, 123.1, 121.3, 114.2, 73.0, 63.0, 62.4, 53.0, 47.4, 33.6, 13.9, 13.8; IR (KBr) $\nu$ 3489, 2982, 1748, 1722, 1643, 1476, 1446, 1368, 1264, 1228, 1216, 1160, 1094, 1070, 1047, 996, 862, 833, 768, 707 $cm^{-1}$; MS ($m/z$, ESI) 532 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{25}H_{27}BrNO_7$ $[M + NH_4]^+$ 532.0965, found 532.0975.

*Diethyl 1-Hydroxy-1-(4-methoxyphenyl)-6-oxo-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2h**).* Yellow solid (47 mg, 54%); mp 113−114 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.24 (d, $J$ = 7.6 Hz, 1H), 7.47−7.32 (m, 5H), 6.81 (d, $J$ = 8.4 Hz, 2H), 5.15 (s, 1H), 4.34−4.08 (m, 4H), 3.76 (s, 3H), 3.38 (d, $J$ = 18.0 Hz, 1H), 3.27 (dd, $J$ = 17.8, 2.2 Hz, 1H), 2.93 (dd, $J$ = 15.2, 2.0 Hz, 1H), 2.24 (d, $J$ = 15.2 Hz, 1H), 1.28−1.22 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.4, 161.9, 158.5, 150.1, 139.2, 135.3, 133.9, 129.4, 127.4, 127.0, 126.2, 121.5, 114.4, 113.8, 72.9, 62.8, 62.3, 55.2, 53.0, 47.7, 33.6, 13.9, 13.8; IR (KBr) $\nu$ 3484, 3437, 3065, 2930, 2851, 1728, 1699, 1643, 1600, 1508, 1477, 1370, 1263, 1244, 1208, 1182, 1082, 1064, 1037, 992, 830, 774, 704 $cm^{-1}$; MS (70 eV, EI) $m/z$ (%) 466 $[M]^+$, 448, 421, 375, 347, 331, 303, 213, 135, 107, 92, 77; HRMS (EI) calcd for $C_{26}H_{26}O_8$ $[M]^+$ 466.1628, found 466.1634.

*Diethyl 1-(4-Chlorophenyl)-1-hydroxy-6-oxo-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2i**).* White solid (71 mg, 79%); mp 174−175 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.24 (d, $J$ = 7.2 Hz, 1H), 7.43−7.25 (m, 7H), 5.31 (s, 1H), 4.35−4.10 (m, 4H), 3.38 (d, $J$ = 18.0 Hz, 1H), 3.28 (dd, $J$ = 18.0, 2.4 Hz, 1H), 2.93 (dd, $J$ = 14.8, 2.4 Hz, 1H), 2.20 (d, $J$ = 15.2 Hz, 1H), 1.29−1.23 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.2, 161.6, 150.3, 145.7, 134.9, 134.0, 132.9, 129.5, 128.7, 127.6, 126.8, 126.6, 121.5, 113.9, 72.9, 62.9, 62.4, 52.9, 47.4, 33.5, 13.8, 13.7; IR (KBr) $\nu$ 3487, 3445, 2981, 2918, 1728, 1700, 1646, 1488, 1448, 1379, 1264, 1245, 1207, 1184, 1088, 1065, 1048, 996, 866, 825, 804, 771, 706 $cm^{-1}$; MS ($m/z$, ESI) 471 $[M + H]^+$; HRMS (ESI) calcd for $C_{25}H_{24}ClO_7$ $[M + H]^+$ 471.1205, found 471.1213.

*Diethyl 1-Hydroxy-1-(4-nitrophenyl)-6-oxo-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2j**).* White solid (81 mg, 84%); mp 177−178 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.25 (dd, $J$ = 7.6, 1.2 Hz, 1H), 8.15 (d, $J$ = 8.0 Hz, 2H), 7.66 (br s, 2H), 7.42−7.36 (m, 2H), 7.31−7.29 (m, 1H), 5.58 (s, 1H), 4.38−4.13 (m, 4H), 3.43 (d, $J$ = 18.0 Hz, 1H), 3.33 (dd, $J$ = 18.0, 1.6 Hz, 1H), 2.97 (dd, $J$ = 15.2, 2.0 Hz, 1H), 2.18 (d, $J$ = 15.2 Hz, 1H), 1.31−1.25 (m, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.5, 169.0, 161.4, 154.5, 150.7, 147.0, 134.6, 134.2, 129.7, 127.8, 126.3, 126.2, 123.9, 121.5, 113.4, 73.1, 63.1, 62.5, 53.0, 46.9, 33.6, 13.8, 13.7; IR (KBr) $\nu$ 3482, 3438, 2986, 1728, 1647, 1601, 1520, 1479, 1450, 1349, 1312, 1266, 1246, 1209, 1184, 1084, 1013, 997, 858, 703 $cm^{-1}$; MS (70 eV, EI) $m/z$ (%) 481 $[M]^+$, 463, 432, 390, 362, 344, 318, 287, 272, 257, 243, 215, 202, 189, 178, 165, 150, 105, 92, 77; HRMS (EI) calcd for $C_{25}H_{23}NO_9$ $[M]^+$ 481.1373, found 481.1369.

*Diethyl 1-Hydroxy-1-(naphthalen-2-yl)-6-oxo-1,2,4,6-tetrahydro-3H-benzo[c]chromene-3,3-dicarboxylate (**2k**).* Yellow solid (78 mg, 81%); mp 145−146 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.25−8.23 (m, 1H), 8.10 (br s, 1H), 7.82−7.72 (m, 3H), 7.51−7.25 (m, 6H), 5.38 (s, 1H), 4.36−4.05 (m, 4H), 3.45 (d, $J$ = 18.0 Hz, 1H), 3.34 (dd, $J$ = 18.0, 2.0 Hz, 1H), 3.00 (dd, $J$ = 15.2, 2.0 Hz, 1H), 2.33 (d, $J$ = 15.2 Hz, 1H), 1.28 (t, $J$ = 7.2 Hz, 3H), 1.20 (t, $J$ = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 172.6, 169.4, 161.9, 150.3, 144.4, 135.2, 134.0, 133.2, 132.4, 129.4, 128.5, 127.5, 127.4, 126.8, 126.2, 126.0, 124.0, 123.1, 121.5, 114.2, 73.4, 62.8, 62.3, 53.0, 47.4, 33.6, 13.8, 13.7; IR (KBr) $\nu$ 3506, 2988, 1743, 1717, 1643, 1488, 1469, 1369, 1266, 1218, 1186, 1159, 1086, 1033, 999, 824, 751, 693 $cm^{-1}$; MS ($m/z$, ESI) 487 $[M + H]^+$; HRMS (ESI) calcd for $C_{29}H_{27}O_7$ $[M + H]^+$ 487.1751, found 487.1758.

*1-Hydroxy-1-methyl-1,2,3,4-tetrahydro-6H-benzo[c]chromen-6-one (**2l**).* White solid (36 mg, 85%); mp 127−128 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.39 (d, $J$ = 8.4 Hz, 1H), 8.18 (d, $J$ = 7.6 Hz, 1H), 7.66 (t, $J$ = 7.8 Hz, 1H), 7.38 (t, $J$ = 7.6 Hz, 1H), 2.66−2.58 (m, 1H), 2.53−2.49 (m, 1H), 2.24 (br s, 1H), 2.06−2.03 (m, 1H), 1.96−1.90 (m, 2H), 1.85−1.78 (m, 1H), 1.68 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 162.4, 152.9, 136.0, 134.0, 129.7, 127.1, 126.2, 121.0, 115.8, 71.6, 41.9, 28.3, 27.7, 18.7; IR (KBr) $\nu$ 3467, 2981, 2940, 2866, 1695, 1630, 1600, 1558, 1478, 1454, 1389, 1364, 1311, 1248, 1188, 1141, 1089, 1031, 996, 927, 811, 770, 701 $cm^{-1}$; MS (70 eV, EI) $m/z$ (%) 230 $[M]^+$, 215, 197, 184, 174, 159, 141, 128, 115, 103, 89, 77, 63, 43, 41; Anal. Calcd (%) for $C_{14}H_{14}O_3$ C 73.03, H 6.13; found C 72.77, H 6.20.

*1-Hydroxy-1,2,3,4-tetrahydro-6H-benzo[c]chromen-6-one (**2m**).* White solid (30 mg, 69%); mp 133−134 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.27 (d, $J$ = 8.0 Hz, 1H), 7.80−7.74 (m, 2H), 7.50−7.45 (m, 1H), 5.05−5.04 (m, 1H), 2.62−2.58 (m, 2H), 2.14−2.03 (m, 2H), 1.95−1.80 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 162.3, 155.1, 136.8, 134.9, 129.6, 127.4, 122.4, 120.4, 111.7, 62.9, 31.2, 27.5, 16.4; IR (KBr) $\nu$ 3460, 2954, 2931, 2875, 1693, 1648, 1600, 1484, 1395, 1366, 1306, 1272, 1190, 1145, 1077, 998, 940, 801, 731, 694 $cm^{-1}$; MS ($m/z$, ESI) 217 $[M + H]^+$; HRMS (ESI) calcd for $C_{13}H_{13}O_3$ $[M + H]^+$ 217.0859, found 217.0860.

*3-(1-Oxo-1H-isochromen-3-yl)propanal (**3n**).* White solid (24 mg, 58%); mp 71−72 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 9.86 (s, 1H), 8.24 (d, $J$ = 7.6 Hz, 1H), 7.71−7.66 (m, 1H), 7.49−7.45 (m, 1H), 7.37 (d, $J$ = 8.0 Hz, 1H), 6.34 (s, 1H), 2.95−2.85 (m, 4H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 199.9, 162.6, 155.6, 137.1, 134.8, 129.4, 127.9, 125.2, 120.1, 103.8, 40.6, 25.9; IR (KBr) $\nu$ 3073, 2918, 2856, 2765, 1716, 1656, 1480, 1429, 1289, 1159, 1044, 1025, 964, 814, 761, 689 $cm^{-1}$; MS ($m/z$, ESI) 203 $[M + H]^+$; HRMS (ESI) calcd for $C_{12}H_{11}O_3$ $[M + H]^+$ 203.0703, found 203.0703.

*Diethyl 2-((1-Oxo-1H-isochromen-3-yl)methyl)-2-(3-oxo-3-phenylpropyl)malonate (**3o**).* Colorless oil (75 mg, 84%); $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.21 (d, $J$ = 8.0 Hz, 1H), 7.97−7.95 (m, 2H), 7.67 (td, $J$ = 7.6, 1.1 Hz, 1H), 7.55 (t, $J$ = 7.4 Hz, 1H), 7.48−7.43 (m, 3H), 7.35 (d, $J$ = 8.0 Hz, 1H), 6.38 (s, 1H), 4.33−4.19 (m, 4H), 3.25 (s, 2H), 3.11 (t, $J$ = 7.6 Hz, 2H), 2.40 (t, $J$ = 7.8 Hz, 2H), 1.26 (t, $J$ = 7.0 Hz, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 198.5, 170.2, 161.7, 152.7, 136.7, 136.4, 134.7, 133.1, 129.4, 128.5, 128.1, 128.0, 125.3, 120.3, 106.4, 61.8, 56.3, 37.7, 33.8, 27.2, 13.9; IR (KBr) $\nu$ 2981, 1724, 1684, 1656, 1600, 1484, 1448, 1368, 1181, 1091, 1043, 1020, 856, 736, 689 $cm^{-1}$; MS ($m/z$, ESI) 468 $[M + NH_4]^+$; HRMS (ESI) calcd for $C_{26}H_{30}NO_7$ $[M + NH_4]^+$ 468.2017, found 468.2026.

*11-Hydroxyindeno[1,2-c]isochromen-5(11H)-one (**2p**).* White solid (36 mg, 72%); mp 173−174 °C; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.17−8.14 (m, 1H), 7.85 (d, $J$ = 7.6 Hz, 1H), 7.77−7.72 (m, 1H), 7.65 (dd, $J$ = 4.6, 3.4 Hz, 1H), 7.46−7.37 (m, 4H), 5.60 (s, 1H), 2.32 (br s, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 162.6, 154.2, 144.9, 135.3, 135.0, 134.2, 130.9, 129.2, 128.9, 127.6, 124.4, 122.9, 119.6, 119.2, 117.5, 72.3; IR (KBr) $\nu$ 3274, 1748, 1628, 1606, 1486, 1302, 1000, 758 $cm^{-1}$; MS (EI, 70 eV) $m/z$ (%) 250 $[M]^+$, 249, 248, 220, 204, 176, 163, 137, 124, 110, 96, 89, 82, 62, 50; HRMS (ESI) calcd for $C_{16}H_{11}O_3$ $[M + H]^+$ 251.0703, found 251.0705.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00128.

Copies of $^1H$ and $^{13}C$ NMR spectral data for all compounds (PDF)



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### Notes

The authors declare no competing financial interest.

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