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Stereoselective Synthesis of 2,8-Dioxabicyclo[3.3.1]nonane Derivatives via a Sequential Michael Addition/Bicyclization Reaction

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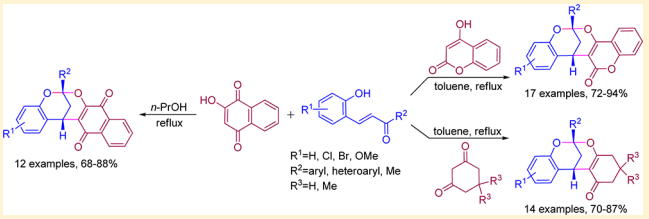
Supporting Information

ABSTRACT: A highly efficient and stereoselective synthesis of coumarin-, 1,3-cyclohexanedione-, and 1,4-naphthoquinone-fused 2,8-dioxabicyclo[3.3.1]nonanes is described. This was achieved via a sequential Michael addition/bicyclization reaction from easily accessible 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives. Three chemical bonds (one C−C bond and two C−O bonds), two six-membered cycles, and two stereogenic centers were formed in a one-pot operation.



INTRODUCTION

Methylene-bridged bicyclic systems, such as Tröger's base[1] and its derivatives have been widely employed as molecular tweezers,[2] ion receptors,[3] and high affinity DNA targeting fluorescent supramolecular scaffolds[4] because of their rigid skeletons. In accordance, a great deal of effort has been devoted to the synthesis of similar types of molecular framework in recent years.[5−7] 2,8-Dioxabicyclo[3.3.1]nonane ring systems, which can be described as the analogues of Tröger's base, are interesting and elaborate V-shaped rigid molecules. Meanwhile, these structural fragments are also embodied in a wide range of natural products, e.g., biflavonoid derivative (**1**), dracoflavan C (**2**), and dracoflavan D (**3**) (Figure 1).[8]

It is well-known that 4-hydroxycoumarin is widely used in organic synthesis for the preparation of many synthetic drugs and drug candidates (such as warfarin, phenprocoumon, brodifacoum, and arisugacin A), all of which have shown excellent biological and pharmacological activities.[9] However, few routes have thus far been reported for the synthesis of coumarin-fused 2,8-dioxabicyclo[3.3.1]nonanes. In 1981, Jurd demonstrated that 1-aryl-substituted 2,8-dioxabicyclo[3.3.1]-nonanes could be synthesized by the reaction of flavylium chloride with 4-hydroxycoumarin (**4**) in warm acetic acid and hydrochloric acid solution (Scheme 1, Path I).[10] Manolov also illustrated a base-catalyzed condensation reaction between 3-benzoylcoumarin (or 3-acetylcoumarin) and 4-hydroxycoumarin to afford the corresponding 1-phenyl (or 1-methyl) 2,8-dioxabicyclo[3.3.1]nonanes (Scheme 1, Path II).[11] Yang reported that these kinds of molecules, which had further potential to act as Vitamin K 2,3-epoxide reductase (VKOR) inhibitors, could be achieved through the reactions of 2-phenylchroman-4-ol with 4-hydroxycoumarin in the presence of aluminum chloride (Scheme 1, Path III).[12] Accordingly, the development of a simple and efficient method toward 2,8-dioxabicyclo[3.3.1]nonanes is still of significant interest. Recently, we reported an efficient synthesis of novel functionalized 2-aryl-4-(indol-3-yl)-4*H*-chromenes by the reactions of 2-hydroxychalcones with substituted indoles in the presence of a catalytic amount of iodine.[13] In a continuation of our efforts to develop new synthetic protocols for building valuable heterocyclic frameworks,[14] we herein describe a highly efficient and stereoselective synthesis of 1-substituted coumarin-fused 2,8-dioxabicyclo[3.3.1]nonanes from easily available staring materials 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives (**5**) and 4-hydroxycoumarin (**4**) (Scheme 1, Path IV). Moreover, 5,5-dimethyl-1,3-cyclohexanedione (**7a**), 1,3-cyclohexanedione (**7b**) and 2-hydroxy-1,4-naphthoquinone (**9**) were also found suitable for the reactions, affording the corresponding 1,3-dione- and 1,4-naphthoquinone-fused 2,8-dioxabicyclo[3.3.1]nonanes in excellent yields with high stereoselectivity.

RESULTS AND DISCUSSION

Initially, an attempted reaction of 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one (**5a**, 0.5 mmol) with 4-hydroxycoumarin (**4**, 0.5 mmol) was carried out under varied conditions. We were pleased to find that the unexpected product coumarin-fused 1-phenyl 2,8-dioxabicyclo[3.3.1]nonane (**6a**) was obtained in excellent yield (94%) in refluxing toluene for 6 h (Table 1, entry 1). The solution became homogeneous as the starting materials were completely dissolved. When the reaction mixture was cooled to room temperature and stood overnight, the yellow crystals of **6a** precipitated and were found to be pure enough for structural analysis. The structure was identified by means of ^{1}H NMR, ^{13}C NMR, IR, and HRMS. The steric

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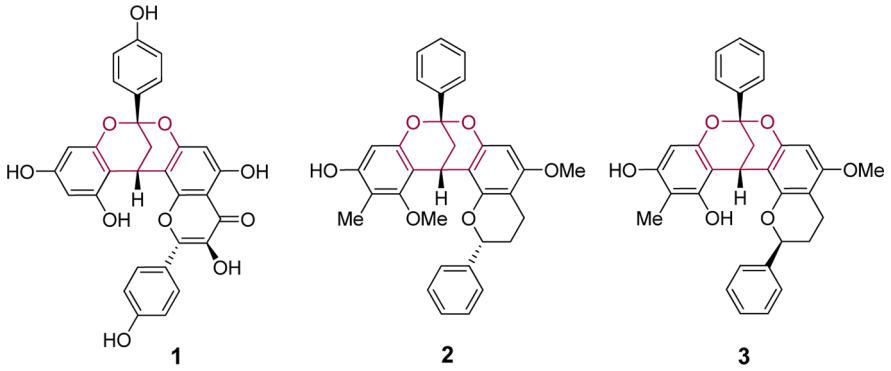


Figure 1. Examples of natural products.

Scheme 1. Strategy for the Synthesis of 2,8-Dioxabicyclo[3.3.1]nonanes

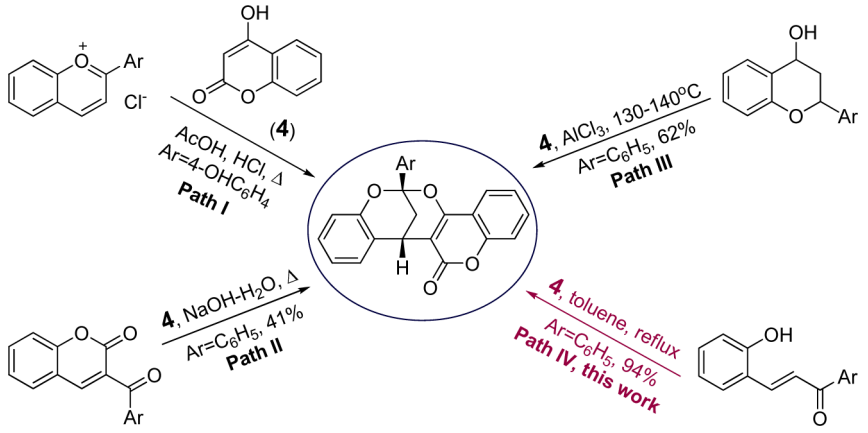
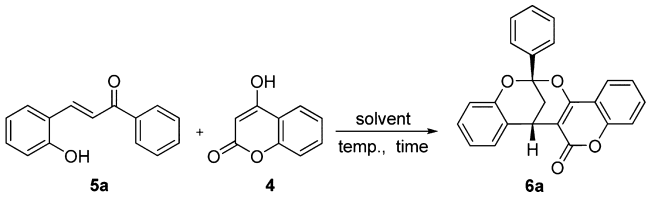


Table 1. Optimization of Reaction Condition for the Synthesis of 6a[a]



entry	solvent	temp (°C)	time (h)	yield (%)[b]
1	toluene	reflux	6	94
2	toluene	80	6	30
3	toluene	60	6	<5
4	THF	reflux	6	0
5	benzene	reflux	6	38
6	MeCN	reflux	10	23
7	MeOH	reflux	10	15
8	EtOH	reflux	10	24
9	*n*-PrOH	reflux	10	93
10	*t*-BuOH	reflux	10	32
11	DMF	110	10	12
12	DMSO	110	10	23

[a]All reactions were performed with **5a** (0.5 mmol) and **4** (0.5 mmol) in solvent (4.0 mL). [b]Isolated yield.

configuration was further clarified by X-ray single-crystal diffraction analysis, which was in accordance with the reported literature (see the Supporting Information).[11] One of the dihydropyran rings fused with the benzopyran ring adopted an *e,f*-diplanar configuration, while the other displayed a similar configuration. Nevertheless, decreasing the reaction temperature resulted in a low yield in toluene, and **6a** was not observed in THF (Table 1, entries 2−4). This transformation was also attempted in other different solvents, such as benzene, MeCN, MeOH, EtOH, *t*-BuOH, DMF and DMSO, but **6a** was only isolated in 12−38% yield (Table 1, entries 5−8, 10−12). It should also be noted that when *n*-PrOH was used as the solvent, the reaction gave the product **6a** in 93% isolated yield (Table 1, entry 9). Considering ease of workup and purification, the optimized reaction conditions were identified as the reaction of **5a** with 1.0 equiv of **4** in toluene at reflux temperature.

With the optimal reaction conditions in hand, we then examined the reactions of 4-hydroxycoumarin with a variety of 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives (**5**), which were synthesized according to the known methods,[13,15] to establish the generality of the present transformation. The results are listed in Scheme 2. The reactions for the substrates bearing electron-donating substituents (−OMe) on the phenyl ring of R^2 performed smoothly to deliver the corresponding **6b** and **6c** in slightly lower yields (80 and 76%). We then expected to introduce the halogen atom into the target molecules, which is known to be readily converted into related important derivatives via classic coupling reactions (Heck, Suzuki, Sonogashira, Liebeskind−Srogl, et al). It was found that the substrates bearing electron-withdrawing halogen-atom (−Cl, −Br and −F) on the phenyl rings delivered the corresponding products **6d−f** in excellent yields (90−93%). Heteroaryl (R^2 = 2-furyl, 2-thienyl) and alkyl group (−Me) substituted substrates were also suitable for the reactions, affording the corresponding products **6g−i** in good yields (75−80%). To our delight, 5-

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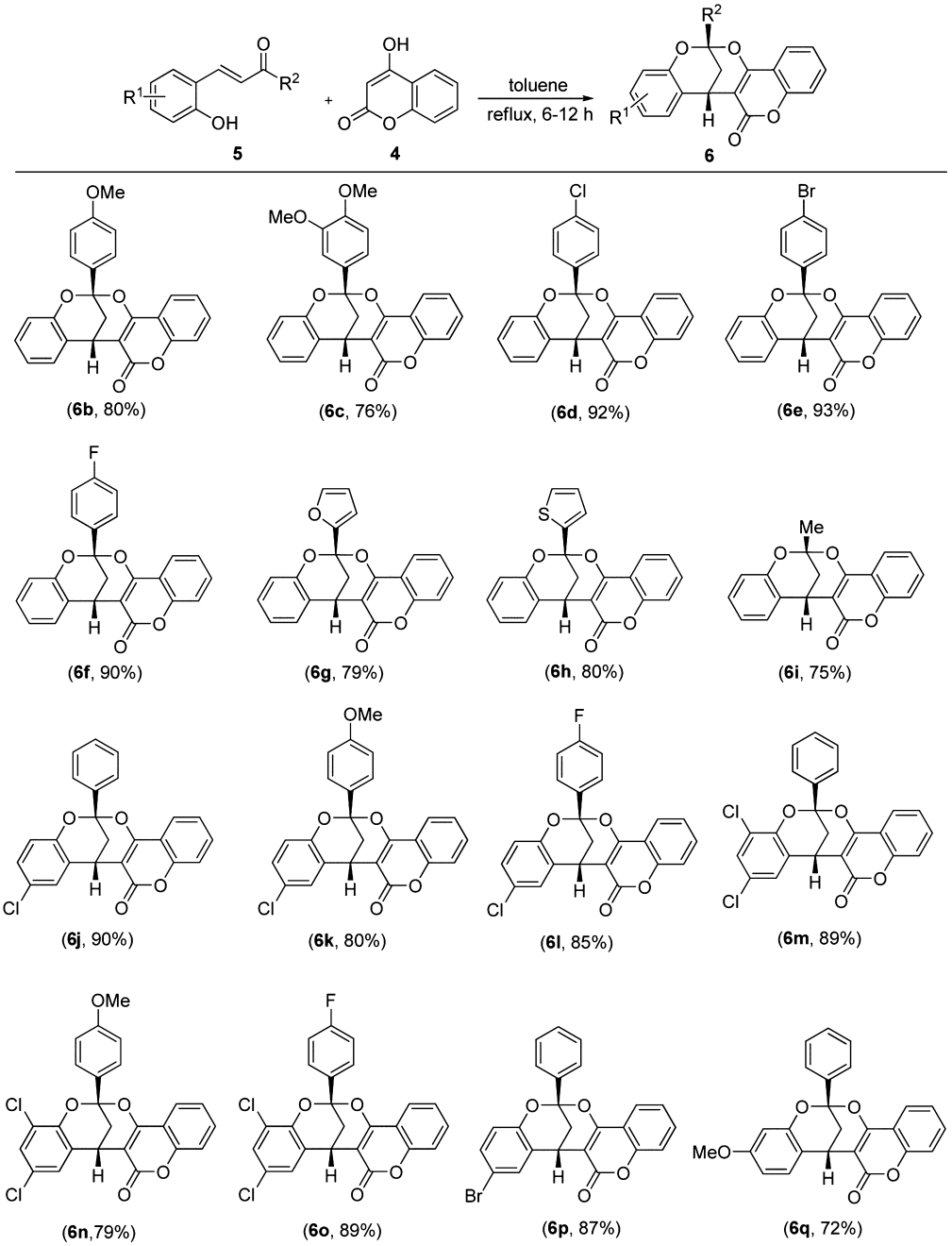
Scheme 2. Synthesis of Coumarin-Fused 2,8-Dioxabicyclo[3.3.1]nonanes[a,b]



[a]All reactions were performed with **4** (0.5 mmol) and **5** (0.5 mmol) in toluene (4.0 mL) at reflux. [b]Isolated yield.

chloro-, 3,5-dichloro-, 5-bromo- and 4-methoxy-substituted 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-ones (R^1) also provided **6j–q** in 72–90% yields.

Encouraged by the results achieved above, we hoped that the substrates of this efficient reaction system could be further extended. Next, 5,5-dimethylcyclohexane-1,3-dione (**7a**) and 1,3-cyclohexanedione (**7b**) were employed to react with 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives under standard reaction conditions. As shown in Scheme 3, electron-rich/deficient aromatic, heterocyclic aromatic and methyl group substrates also gave the corresponding products **8a–n** in good yields (70–87%). In addition, the structure of **8f** was also confirmed by X-ray single-crystal diffraction analysis (see the Supporting Information) and was shown to adopt the same configuration as the analogous in literatures.[16,17]

Naphthoquinones and quinones are ubiquitous in nature and have been found to have a wide range of biological activities, including cytotoxicity to cancer cells.[18] The involvement of naphthoquinone moieties in Michael-type addition reactions are widely studied in organic synthesis.[19,20] A literature survey revealed that there are no examples for the preparation of naphthoquinone-fused 2,8-dioxabicyclo[3.3.1]nonane derivatives. Consequently, 2-hydroxy-1,4-naphthoquinone (**9**) was also used to react with 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives in *n*-PrOH at reflux. As shown in Scheme 4, the corresponding products **10a–i** were isolated in good yields (68–88%) when R^2 was electron-rich/deficient aromatic,

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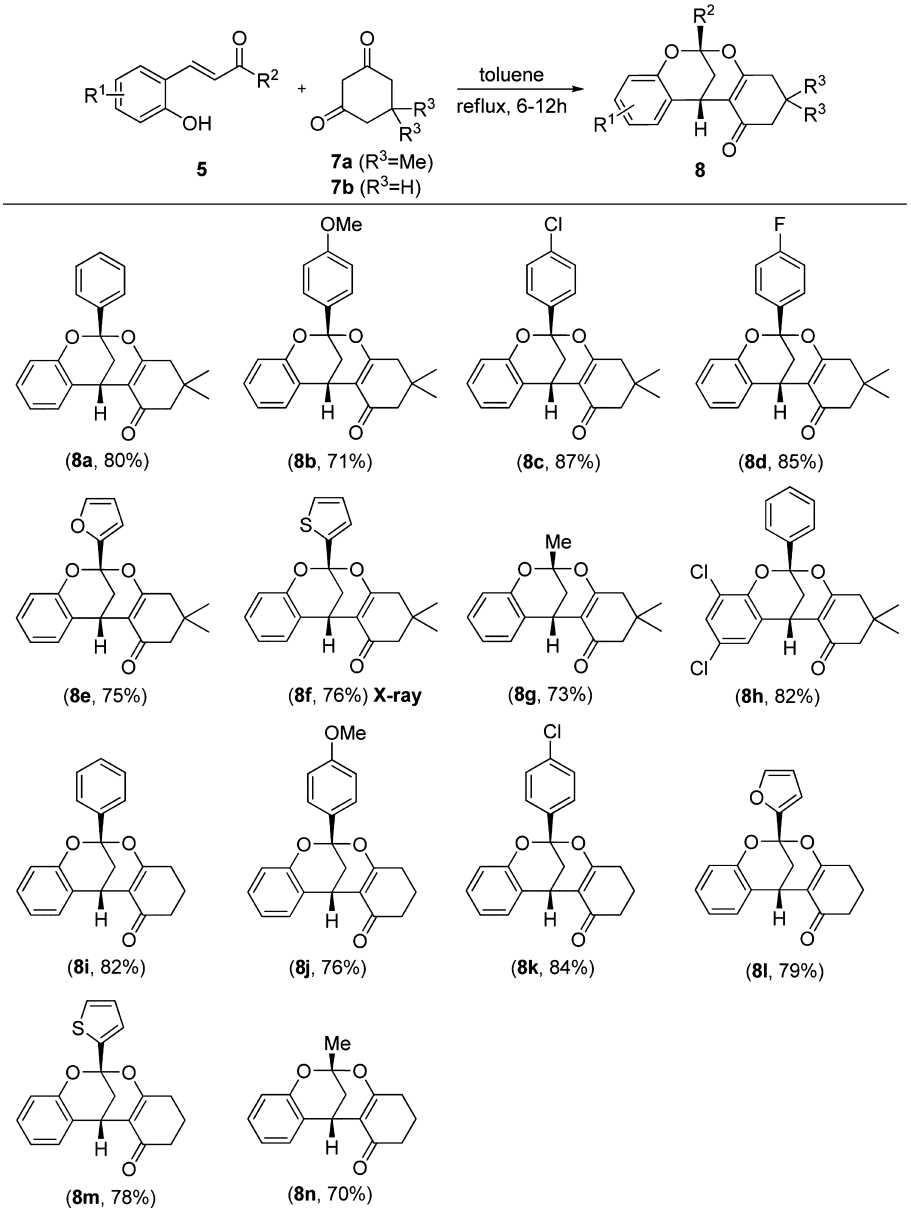
Scheme 3. Synthesis of 1,3-Cyclohexanedione-Fused 2,8-Dioxabicyclo[3.3.1]nonanes[a,b]



[a]All reactions were performed with **5** (0.5 mmol) and **7** (0.5 mmol) in toluene (4.0 mL) at reflux. [b]Isolated yield

heterocyclic aromatic and methyl substituted groups. Moreover, chlorine- and bromine-substituted substrates (R^1 = Cl, Br) were also suitable for this reaction, affording the corresponding products **10j–l** in 78–83% yields.

However, when the mixture of **5a** and noncyclic pentane-2,4-dione (**11**) was heated at reflux for 10 h, the corresponding 2,8-dioxabicyclo[3.3.1]nonane product was not observed, but 3-(2-phenyl-4*H*-chromen-4-yl)pentane-2,4-dione (**12**) was isolated in 71% yield (Scheme 5).

Moreover, it was found that no reaction occurred when the mixture of 4-hydroxycoumarin (**4**) and 1,3-diphenyl-2-propen-1-one (chalcone) was heated in refluxing toluene for 16 h,[21] which indicated that the reaction was obviously affected by the hydroxy (−OH), probably because of the acidity of the proton. Therefore, the present reactions can be regarded as a self-catalyzed process. Subsequently, a possible reaction mechanism was proposed as shown in Scheme 6 (using **6a** as an example). First, 4-hydroxycoumarin reacted with 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one (**5a**) to form intermediate **I** through a Michael addition reaction.[22] Then intramolecular cyclization of intermediate **I** gave two possible hemiketal-form intermediate **II** or **III**,[13,20a,23,24] both of which afforded the same target product **6a** via a spontaneous intramolecular cyclization process after loss of water.[10,11]

CONCLUSIONS

In summary, we have described a highly efficient and stereoselective construction of coumarin-, 1,3-cyclohexanedione- and 1,4-naphthoquinone-fused 2,8-dioxabicyclo[3.3.1]-nonanes via a sequential Michael addition/bicyclization reaction from 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives. Three chemical bonds (one C–C bond and two C–O bonds), two six-membered cycles, and two stereogenic centers were formed in a one-pot operation. Easily accessible

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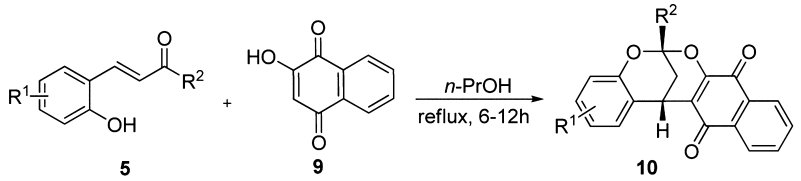
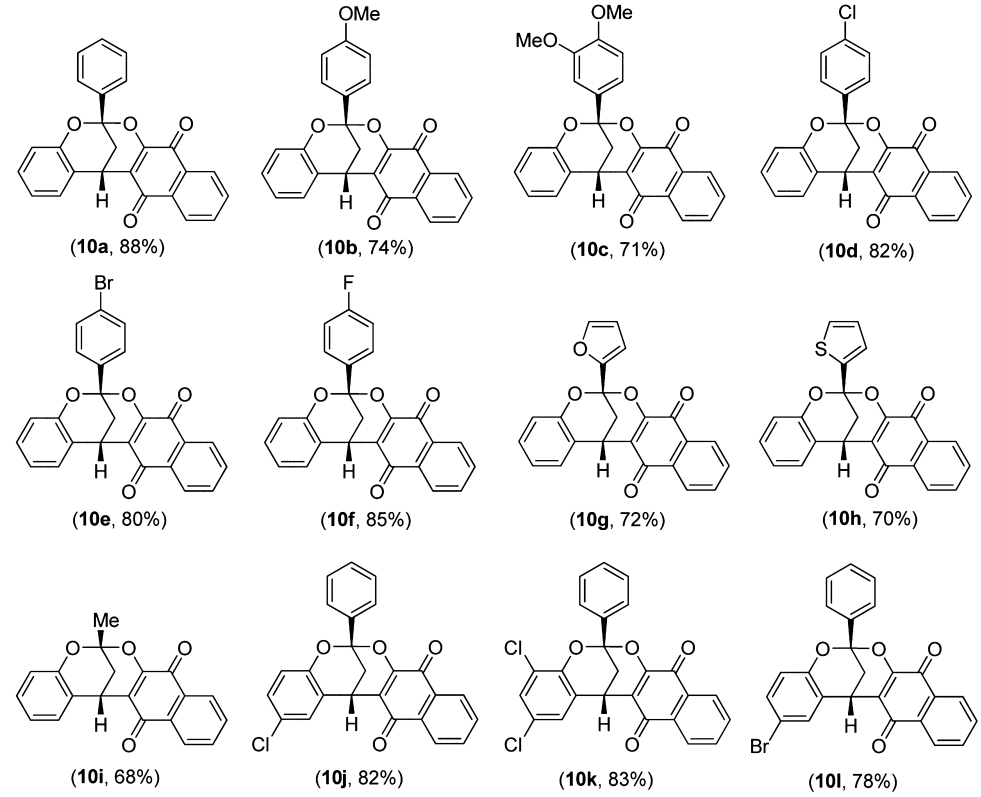
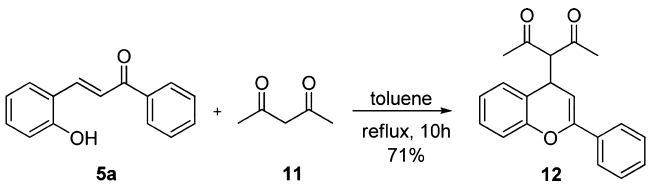
Scheme 4. Synthesis of 1,4-Naphthoquinone-Fused 2,8-Dioxabicyclo[3.3.1]nonanes[a,b]





[a]All reactions were performed with **5** (0.5 mmol) and **9** (0.5 mmol) in *n*-PrOH (4.0 mL) at reflux. [b]Isolated yield.

Scheme 5



starting materials, a wide scope of substrates, excellent yields and ease of purification (no column chromatography) were the main advantages of this reaction.

EXPERIMENTAL SECTION

General Experimental Details. All substrates and reagents were commercially available and used without further purification. IR spectra were recorded as KBr pellets with absorption in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on 300 MHz spectrometers using $CDCl_3$ as the solvent. Chemical shifts are reported relative to TMS (internal standard). High resolution mass spectra were recorded on TOF-QII (ESI). Mass spectra was recorded on ESI or EI (70 eV). Melting points were determined using an electrothermal capillary melting point apparatus and not corrected.

General Procedure for the Synthesis of 6. A mixture of 4-hydroxycoumarin (**4**, 81 mg, 0.5 mmol) and 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives (**5**, 0.5 mmol) was heated at reflux in anhydrous toluene in a sealed tube (4.0 mL). The solution became homogeneous as the starting materials were completely dissolved. After the reactant disappeared (6−12 h, monitored by thin layer chromatography), the mixture was cooled to room temperature and stood overnight. Thus the crystals were precipitated, filtrated and washed with a small amount of anhydrous ethanol, and the target products **6** were obtained as the yellow solids.

Compound ***6a***. Yellow solid: 173 mg, 94% yield; mp 234−235 °C; IR (KBr, cm^{-1}) 3441, 2358, 1706, 1630, 1486, 1393, 1233, 1117, 1019, 760; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.85 (d, J = 7.6 Hz, 1H), 7.77−7.75 (m, 2H), 7.56−7.45 (m, 5H), 7.31−7.17 (m, 3H), 7.07−6.96 (m, 2H), 4.39 (s, 1H), 2.46−2.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.5, 158.2, 152.4, 151.3, 139.7, 131.9, 129.4, 128.6, 128.3, 128.2, 125.6, 125.1, 124.0, 122.7, 122.1, 116.6, 116.3, 115.0, 106.0, 100.2, 32.9, 27.1; ESI-MS m/z 369.17 $[M + H]^+$.

Compound ***6b***. Yellow solid: 159 mg, 80% yield; mp 188−189 °C; IR (KBr, cm^{-1}) 3441, 2359, 1716, 1628, 1513, 1390, 1245, 1114, 1029, 760; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.86 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.7 Hz, 2H), 7.55−7.48 (m, 2H), 7.31−7.17 (m, 3H), 7.06−6.96 (m, 4H), 4.39 (s, 1H), 3.88 (s, 3H), 2.45−2.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.7, 160.3, 158.4, 152.4, 151.4, 132.0, 131.9, 128.3, 128.2, 127.0, 125.1, 124.0, 122.7, 122.0, 116.7, 116.3, 115.1, 113.9, 106.0, 100.3, 55.4, 32.9, 27.3; ESI-MS m/z 399.15 $[M + H]^+$.

Compound ***6c***. Yellow solid: 172 mg, 76% yield; mp 194−195 °C; IR (KBr, cm^{-1}) 3438, 2943, 1709, 1631, 1517, 1454, 1391, 1267, 1226,

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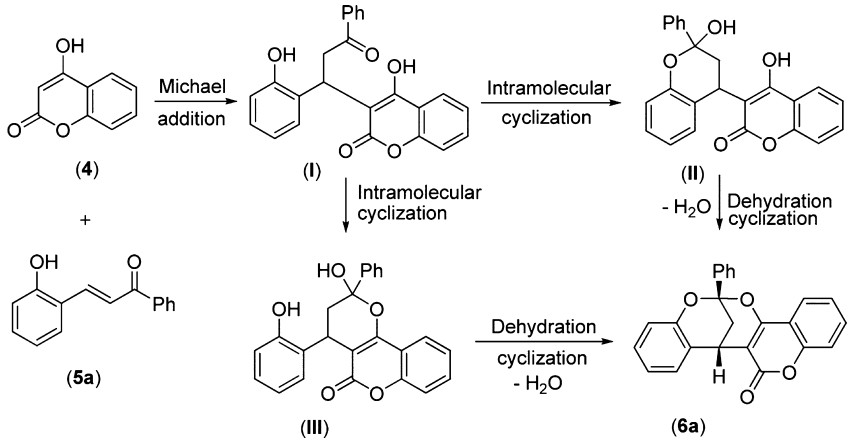
Scheme 6. Possible Reaction Mechanism



1116, 1028, 761; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.85 (d, J = 7.7 Hz, 1H), 7.56−7.48 (m, 2H), 7.34−7.17 (m, 5H), 7.07−6.97 (m, 3H), 4.40 (s, 1H), 3.95 (s, 6H), 2.48−2.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.5, 158.2, 152.3, 151.3, 149.8, 148.9, 132.2, 131.9, 128.3, 128.2, 125.1, 124.0, 122.6, 122.1, 118.2, 116.7, 116.3, 115.1, 110.8, 109.0, 106.0, 100.2, 56.04, 55.98, 32.9, 27.2; HRMS (ESI) calcd for $C_{26}H_{21}O_6$ $[M + H]^+$ 429.1333, found 429.1318.

Compound ***6d***. Yellow solid: 185 mg, 92% yield; mp 223−224 °C; IR (KBr, cm^{-1}) 3410, 1715, 1631, 1489, 1390, 1330, 1232, 1118, 1014, 884, 821, 761; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.83 (d, J = 7.9 Hz, 1H), 7.70 (d, J = 8.6 Hz, 2H), 7.56−7.46 (m, 4H), 7.30−7.17 (m, 3H), 7.06−6.97 (m, 2H), 4.40−4.38 (m, 1H), 2.47−2.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.4, 158.0, 152.3, 151.1, 138.2, 135.4, 132.0, 128.8, 128.4, 128.2, 127.2, 124.9, 124.1, 122.6, 122.2, 116.7, 116.3, 114.9, 106.0, 99.9, 32.8, 27.1; HRMS (ESI) calcd for $C_{24}H_{16}ClO_4$ $[M + H]^+$ 403.0732, found 403.0712.

Compound ***6e***. Yellow solid: 208 mg, 93% yield; mp 220−221 °C; IR (KBr, cm^{-1}) 3440, 1715, 1632, 1488, 1390, 1232, 1116, 1012, 884, 819, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.84 (d, J = 7.8 Hz, 1H), 7.64−7.50 (m, 6H), 7.32−7.18 (m, 3H), 7.06−6.97 (m, 2H), 4.40 (s, 1H), 2.42−2.36 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.4, 158.0, 152.3, 151.1, 138.8, 132.0, 131.8, 128.4, 128.2, 127.5, 124.9, 124.1, 123.7, 122.6, 122.3, 116.7, 116.3, 114.9, 106.0, 99.9, 32.7, 27.0; HRMS (ESI) calcd for $C_{24}H_{16}BrO_4$ $[M + H]^+$ 447.0226, found 447.0236.

Compound ***6f***. Yellow solid: 174 mg, 90% yield; mp 222−223 °C; IR (KBr, cm^{-1}) 3425, 1715, 1631, 1501, 1391, 1332, 1231, 1115, 1021, 885, 826, 761; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.84 (d, J = 7.7 Hz, 1H), 7.77−7.73 (m, 2H), 7.56−7.48 (m, 2H), 7.31−7.16 (m, 5H), 7.06−6.97 (m, 2H), 4.40 (s, 1H), 2.44−2.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 163.3 (d, $^1J_{CF}$ = 247.2 Hz), 161.5, 158.1, 152.4, 151.2, 135.7 (d, $^4J_{CF}$ = 3.2 Hz), 132.0, 128.4, 128.2, 127.7 (d, $^3J_{CF}$ = 8.3 Hz), 125.0, 124.1, 122.6, 122.2, 116.7, 116.3, 115.5 (d, $^2J_{CF}$ = 21.6 Hz), 115.0, 106.0, 100.0, 33.0, 27.2; HRMS (ESI) calcd for $C_{24}H_{16}FO_4$ $[M + H]^+$ 387.1027, found 387.1036.

Compound ***6g***. Yellow solid: 142 mg, 79% yield; mp 204−206 °C; IR (KBr, cm^{-1}) 3437, 1710, 1633, 1488, 1391, 1222, 1117, 1022, 877, 759; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.81 (d, J = 7.7 Hz, 1H), 7.53−7.45 (m, 3H), 7.28−7.15 (m, 3H), 7.01−6.95 (m, 2H), 6.82 (d, J = 2.7 Hz, 1H), 6.52 (s, 1H), 4.41 (s, 1H), 2.60−2.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.4, 157.7, 152.3, 150.8, 150.7, 143.3, 132.0, 128.3, 128.2, 124.9, 124.0, 122.8, 122.2, 116.6, 116.3, 114.8, 110.6, 108.3, 106.0, 96.6, 29.5, 26.3; HRMS (ESI) calcd for $C_{22}H_{15}O_5$ $[M + H]^+$ 359.0914, found 359.0914.

Compound ***6h***. Yellow solid: 150 mg, 80% yield; mp 218−219 °C; IR (KBr, cm^{-1}) 3403, 1708, 1633, 1487, 1391, 1330, 1231, 1116, 1030, 982, 761; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.85 (d, J = 7.6 Hz, 1H), 7.55−7.43 (m, 3H), 7.37 (d, J = 3.3 Hz, 1H), 7.30−7.10 (m, 4H), 7.03−6.96 (m, 2H), 4.41 (s, 1H), 2.66−2.53 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.6, 158.0, 152.3, 150.9, 142.8, 132.1, 128.4, 128.2, 127.1, 126.6, 125.5, 124.8, 124.1, 122.8, 122.3, 116.6, 116.4, 114.8, 105.9, 99.2, 33.0, 27.1; HRMS (ESI) calcd for $C_{22}H_{15}O_4S$ $[M + H]^+$ 375.0686, found 375.0683.

Compound ***6i***. Yellow solid: 115 mg, 75% yield; mp 254−255 °C; IR (KBr, cm^{-1}) 3445, 1703, 1628, 1487, 1446, 1390, 1142, 1035, 862, 762; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.78 (d, J = 7.8 Hz, 1H), 7.48−7.42 (m, 2H), 7.24−7.19 (m, 2H), 7.15−7.10 (m, 1H), 6.94−6.86 (m, 2H), 4.30 (s, 1H), 2.34−2.19 (m, 2H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.6, 158.0, 152.2, 151.1, 131.8, 128.09, 128.07, 125.0, 123.8, 122.7, 121.6, 116.5, 116.0, 114.9, 105.7, 99.7, 30.7, 26.7, 26.6; ESI-MS m/z 307.17 $[M + H]^+$.

Compound ***6j***. Yellow solid: 181 mg, 90% yield; mp 194−195 °C; IR (KBr, cm^{-1}) 3441, 2356, 1705, 1628, 1482, 1391, 1237, 1117, 1012, 883, 826, 758; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.89 (d, J = 7.9 Hz, 1H), 7.87−7.73 (m, 2H), 7.57−7.50 (m, 5H), 7.34−7.26 (m, 2H), 7.17−7.13 (m, 1H), 6.98 (d, J = 8.7 Hz, 1H), 4.36 (t, J = 3.0 Hz, 1H), 2.44 (d, J = 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.4, 158.3, 152.5, 150.0, 139.3, 132.2, 129.6, 128.7, 128.3, 127.8, 127.0, 126.6, 125.6, 124.2, 122.8, 117.6, 116.8, 114.9, 105.4, 100.3, 32.6, 27.1; HRMS (ESI) calcd for $C_{24}H_{16}ClO_4$ $[M + H]^+$ 403.0732, found 403.0726.

Compound ***6k***. Yellow solid: 173 mg, 80% yield; mp 206−207 °C; IR (KBr, cm^{-1}) 3439, 1711, 1629, 1511, 1481, 1394, 1340, 1249, 1174, 1119, 1030, 880, 825, 763; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.84 (d, J = 7.3 Hz, 1H), 7.66 (d, J = 8.8 Hz, 2H), 7.54−7.49 (m, 2H), 7.31−7.23 (m, 2H), 7.15−7.11 (m, 1H), 7.03−6.94 (m, 3H), 4.34−4.24 (m, 1H), 3.87 (s, 3H), 2.42−2.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.4, 160.4, 158.3, 152.4, 150.0, 132.1, 131.4, 128.2, 127.7, 126.9, 126.8, 126.7, 124.1, 122.7, 117.6, 116.7, 114.9, 113.9, 105.3, 100.3, 55.4, 32.6, 27.1; HRMS (ESI) calcd for $C_{25}H_{18}ClO_5$ $[M + H]^+$ 433.0837, found 433.0838.

Compound ***6l***. Yellow solid: 178 mg, 85% yield; mp 203−204 °C; IR (KBr, cm^{-1}) 3428, 2359, 1721, 1637, 1481, 1392, 1339, 1229, 1148, 1127, 1015, 890, 831, 752; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.83 (d, J = 7.5 Hz, 1H), 7.75−7.71 (m, 2H), 7.57−7.51 (m, 2H), 7.34−7.13 (m, 5H), 6.97 (d, J = 8.7 Hz, 1H), 4.36 (t, J = 3.0 Hz, 1H), 2.42 (d, J = 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 163.3 (d, $^1J_{CF}$ = 247.3 Hz), 161.3, 158.2, 152.4, 149.8, 135.3 (d, $^4J_{CF}$ = 3.2 Hz), 132.3, 128.4, 127.8, 127.7 (d, $^3J_{CF}$ = 8.5 Hz), 127.1, 126.5, 124.2, 122.7, 117.6, 116.8, 115.6 (d, $^2J_{CF}$ = 21.8 Hz), 114.8, 105.4, 100.0, 32.6, 27.1; HRMS (ESI) calcd for $C_{24}H_{15}ClFO_4$ $[M + H]^+$ 421.0637, found 421.0642.

Compound ***6m***. Yellow solid: 194 mg, 89% yield; mp 229−230 °C; IR (KBr, cm^{-1}) 3429, 2359, 1718, 1637, 1452, 1393, 1331, 1263, 1116, 1039, 1015, 995, 921, 758; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.88−7.78 (m, 3H), 7.57−7.46 (m, 5H), 7.34−7.25 (m, 3H), 4.37 (t, J = 2.9 Hz, 1H), 2.52 (dd, J_1 = 13.8 Hz, J_2 = 2.9 Hz, 1H), 2.36 (dd, J_1 = 13.8 Hz, J_2 = 2.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.3, 158.3, 152.5, 146.1, 138.7, 132.4, 129.7, 128.74, 128.68, 127.9, 126.9, 126.3, 125.7, 124.2, 122.9, 122.1, 116.8, 114.7, 104.7, 100.6,

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32.5, 27.3; HRMS (ESI) calcd for $C_{24}H_{15}Cl_2O_4$ $[M + H]^+$ 437.0342, found 437.0345.

Compound ***6n***. Yellow solid: 184 mg, 79% yield; mp 226−227 °C; IR (KBr, cm^{-1}) 3413, 2966, 1712, 1623, 1451, 1393, 1334, 1249, 1186, 1102, 1032, 921, 758; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.84 (d, J = 7.9 Hz, 1H), 7.71 (d, J = 8.7 Hz, 2H), 7.55−7.51 (m, 1H), 7.45 (d, J = 2.3 Hz, 1H), 7.33−7.24 (m, 3H), 7.03 (d, J = 8.7 Hz, 2H), 4.37−4.35 (m, 1H), 3.88 (s, 3H), 2.50 (dd, J_1 = 13.8 Hz, J_2 = 3.1 Hz, 1H), 2.34 (dd, J_1 = 13.8 Hz, J_2 = 2.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.3, 160.5, 158.4, 152.5, 146.2, 132.3, 130.8, 128.6, 128.0, 127.1, 126.8, 126.3, 124.2, 122.9, 122.1, 116.7, 114.7, 114.0, 104.6, 100.7, 55.4, 32.5, 27.4; HRMS (ESI) calcd for $C_{25}H_{17}Cl_2O_5$ $[M + H]^+$ 467.0448, found 467.0445.

Compound ***6o***. Yellow solid: 202 mg, 89% yield; mp 202−203 °C; IR (KBr, cm^{-1}) 3441, 1714, 1628, 1503, 1451, 1393, 1334, 1236, 1157, 1101, 1037, 925, 882, 763; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.86−7.76 (m, 3H), 7.58−7.53 (m, 1H), 7.47 (d, J = 2.4 Hz, 1H), 7.35−7.18 (m, 5H), 4.39−4.37 (m, 1H), 2.51 (dd, J_1 = 13.7 Hz, J_2 = 3.2 Hz, 1H), 2.35 (dd, J_1 = 13.7 Hz, J_2 = 2.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 163.4 (d, $^1J_{CF}$ = 247.7 Hz), 161.2, 158.2, 152.5, 146.0, 134.7 (d, $^4J_{CF}$ = 3.2 Hz), 132.5, 128.7, 127.9 (d, $^3J_{CF}$ = 8.5 Hz), 127.8, 127.1, 126.3, 124.3, 122.8, 122.1, 116.8, 115.8 (d, $^2J_{CF}$ = 21.8 Hz), 114.6, 104.7, 100.3, 32.5, 27.3; HRMS (ESI) calcd for $C_{24}H_{14}Cl_2FO_4$ $[M + H]^+$ 455.0248, found 455.0250.

Compound ***6p***. Yellow solid: 195 mg, 87% yield; mp 212−213 °C; IR (KBr, cm^{-1}) 3427, 1716, 1634, 1483, 1392, 1337, 1233, 1118, 996, 875, 818, 759; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.88−7.85 (m, 1H), 7.75−7.67 (m, 3H), 7.55−7.50 (m, 4H), 7.33−7.26 (m, 3H), 6.92 (d, J = 8.6 Hz, 1H), 4.37−4.34 (m, 1H), 2.43 (d, J = 3.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.3, 158.3, 152.4, 150.5, 139.2, 132.2, 131.2, 130.6, 129.6, 127.2, 125.6, 124.1, 122.7, 118.1, 116.8, 114.9, 114.3, 105.4, 100.2, 32.5, 27.0; HRMS (ESI) calcd for $C_{24}H_{16}BrO_4$ $[M + H]^+$ 447.0226, found 447.0229.

Compound ***6q***. Yellow solid: 143 mg, 72% yield; mp 177−178 °C; IR (KBr, cm^{-1}) 3440, 1720, 1621, 1243, 1118, 1034; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.88 (d, J = 7.9 Hz, 1H), 7.78−7.75 (m, 2H), 7.54−7.42 (m, 5H), 7.32−7.24 (m, 2H), 6.64−6.54 (m, 2H), 4.36−4.34 (m, 1H), 3.76 (s, 3H), 2.50−2.38 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 161.6, 159.8, 158.0, 152.3, 152.1, 139.7, 131.9, 129.4, 128.6, 128.5, 125.6, 124.0, 122.7, 117.4, 116.7, 115.1, 108.2, 106.5, 101.9, 100.2, 55.4, 33.2, 26.5; MS (EI, 70 eV) m/z (%) 398.16 (100), 279.09 (19), 275.09 (17), 237.08 (43), 224.09 (57), 199.22 (13).

General Procedure for the Synthesis of 8. A mixture of 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives (**5**, 0.5 mmol) and 5,5-dimethylcyclohexane-1,3-dione/cyclohexane-1,3-dione (**7**, 0.5 mmol) was heated at reflux in anhydrous toluene in a sealed tube (4.0 mL). The solution became homogeneous as the starting materials were completely dissolved. After the reactant disappeared (6−12 h, monitored by thin layer chromatography), the mixture was cooled to room temperature, and toluene was removed under reduced pressure. Then, the residue was recrystallized from the mixture of ethanol/hexane to give the target products **8** as the yellow solids.

Compound ***8a***. Yellow solid: 138 mg, 80% yield; mp 161−162 °C; IR (KBr, cm^{-1}) 3443, 2951, 1629, 1381, 1236, 1108, 1023, 883, 761; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.67−7.64 (m, 2H), 7.48−7.37 (m, 4H), 7.16−7.12 (m, 1H), 7.01 (d, J = 8.0 Hz, 1H), 6.93−6.88 (m, 1H), 4.22 (s, 1H), 2.39 (s, 2H), 2.29−2.13 (m, 4H), 1.10 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.7, 167.5, 151.4, 140.2, 129.0, 128.4, 128.0, 127.5, 126.5, 125.5, 121.5, 116.0, 115.4, 99.8, 50.4, 41.6, 33.0, 32.4, 28.8, 27.8, 25.1; HRMS (ESI) calcd for $C_{23}H_{23}O_3$ $[M + H]^+$ 347.1642, found 347.1643.

Compound ***8b***. Yellow solid: 134 mg, 71% yield; mp 113−114 °C; IR (KBr, cm^{-1}) 3445, 2951, 1624, 1515, 1472, 1383, 1332, 1243, 1172, 1105, 1033, 883, 836, 755; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.60−7.55 (m, 2H), 7.38 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.16−7.10 (m, 1H), 7.00−6.88 (m, 4H), 4.22−4.20 (m, 1H), 3.84 (s, 3H), 2.38 (s, 2H), 2.28−2.12 (m, 4H), 1.09 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.8, 167.7, 160.1, 151.5, 132.5, 128.0, 127.5, 126.9, 126.5, 121.5, 115.9, 115.3, 113.7, 99.8, 55.3, 50.3, 41.6, 33.0, 32.4, 28.7, 27.8, 25.2; HRMS (ESI) calcd for $C_{24}H_{25}O_4$ $[M + H]^+$ 377.1747, found 377.1745.

Compound ***8c***. Yellow solid: 166 mg, 87% yield; mp 144−145 °C; IR (KBr, cm^{-1}) 3441, 2950, 1629, 1483, 1329, 1231, 1101, 1023, 884, 835, 756; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.61−7.57 (m, 2H), 7.44−7.37 (m, 3H), 7.17−7.12 (m, 1H), 7.00−6.89 (m, 2H), 4.23−4.21 (m, 1H), 2.39 (s, 2H), 2.29−2.10 (m, 4H), 1.10 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.7, 167.3, 151.2, 138.8, 135.1, 128.6, 128.1, 127.6, 127.1, 126.3, 121.7, 115.9, 115.4, 99.4, 50.4, 41.5, 32.9, 32.4, 28.7, 27.9, 25.1; HRMS (ESI) calcd for $C_{23}H_{22}ClO_3$ $[M + H]^+$ 381.1252, found 381.1254.

Compound ***8d***. Yellow solid: 154 mg, 85% yield; mp 136−137 °C; IR (KBr, cm^{-1}) 3441, 2953, 1630, 1511, 1480, 1383, 1331, 1229, 1157, 1106, 1034, 884, 841, 756; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.66−7.61 (m, 2H), 7.40−7.37 (m, 1H), 7.16−7.10 (m, 3H), 7.00−6.89 (m, 2H), 4.22 (s, 1H), 2.39 (s, 2H), 2.29−2.11 (m, 4H), 1.10 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.7, 167.3, 163.1 (d, $^1J_{CF}$ = 246.6 Hz), 151.3, 136.2 (d, $^4J_{CF}$ = 3.1 Hz), 128.1, 127.7 (d, $^3J_{CF}$ = 8.2 Hz), 127.6, 126.3, 121.7, 115.9, 115.4, 115.3 (d, $^2J_{CF}$ = 21.6 Hz), 99.5, 50.4, 41.6, 33.1, 32.4, 28.7, 27.8, 25.1; HRMS (ESI) calcd for $C_{23}H_{22}FO_3$ $[M + H]^+$ 365.1547, found 365.1553.

Compound ***8e***. Yellow solid: 126 mg, 75% yield; mp 157−158 °C; IR (KBr, cm^{-1}) 3439, 2962, 1626, 1382, 1230, 1113, 1017, 864, 757; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.48 (s, 1H), 7.36 (d, J = 7.1 Hz, 1H), 7.14−7.09 (m, 1H), 6.97−6.88 (m, 2H), 6.68 (d, J = 2.3 Hz, 1H), 6.45 (s, 1H), 4.24 (s, 1H), 2.50−2.15 (m, 6H), 1.07 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.7, 167.0, 151.6, 150.8, 143.0, 128.1, 127.6, 126.3, 121.7, 116.0, 115.4, 110.4, 107.7, 96.2, 50.3, 41.4, 32.3, 29.6, 28.7, 27.8, 24.2; HRMS (ESI) calcd for $C_{21}H_{21}O_4$ $[M + H]^+$ 337.1434, found 337.1432.

Compound ***8f***. Yellow solid: 134 mg, 76% yield; mp 163−164 °C; IR (KBr, cm^{-1}) 3443, 2945, 1630, 1383, 1231, 1105, 1036, 881, 839, 762, 718; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.37 (d, J = 6.0 Hz, 2H), 7.28−7.26 (m, 1H), 7.16−7.04 (m, 2H), 6.98−6.88 (m, 2H), 4.25−4.15 (m, 1H), 2.45−2.15 (m, 6H), 1.08 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.7, 167.2, 151.1, 143.6, 128.0, 127.6, 126.8, 126.2, 125.1, 121.7, 116.0, 115.7, 115.4, 98.6, 50.3, 41.5, 33.1, 32.4, 28.7, 27.8, 25.1; HRMS (ESI) calcd for $C_{21}H_{21}O_3S$ $[M + H]^+$ 353.1206, found 353.1212.

Compound ***8g***. Yellow solid: 104 mg, 73% yield; mp 138−139 °C; IR (KBr, cm^{-1}) 3440, 2949, 1619, 1476, 1382, 1252, 1139, 1063, 854, 832, 754; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.31 (d, J = 7.1 Hz, 1H), 7.10−7.04 (m, 1H), 6.86−6.81 (m, 2H), 4.13 (s, 1H), 2.26 (s, 2H), 2.16−2.07 (m, 3H), 1.98−1.93 (m, 1H), 1.81 (s, 3H), 1.04 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.7, 167.5, 151.2, 128.0, 127.3, 126.4, 121.1, 115.7, 115.2, 99.2, 50.3, 41.6, 32.3, 31.0, 28.7, 27.8, 26.7, 24.7; HRMS (ESI) calcd for $C_{18}H_{21}O_3$ $[M + H]^+$ 285.1485, found 285.1485.

Compound ***8h***. Yellow solid: 170 mg, 82% yield; mp 118−119 °C; IR (KBr, cm^{-1}) 3425, 2958, 1630, 1454, 1383, 1250, 1109, 1041, 917, 869, 761, 689; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.70−7.67 (m, 2H), 7.50−7.43 (m, 3H), 7.37 (d, J = 2.5 Hz, 1H), 7.22 (d, J = 2.5 Hz, 1H), 4.21−4.19 (m, 1H), 2.41 (s, 2H), 2.31−2.11 (m, 4H), 1.11 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.5, 167.7, 146.2, 139.2, 129.34, 129.29, 128.5, 127.9, 126.3, 126.2, 125.6, 121.7, 114.1, 100.2, 50.3, 41.4, 32.5, 32.4, 28.9, 27.7, 25.3; HRMS (ESI) calcd for $C_{23}H_{21}Cl_2O_3$ $[M + H]^+$ 415.0862, found 415.0853.

Compound ***8i***. Yellow solid: 131 mg, 82% yield; mp 126−127 °C; IR (KBr, cm^{-1}) 3445, 2946, 1625, 1382, 1237, 1108, 1026, 877, 758; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.68−7.64 (m, 2H), 7.43−7.39 (m, 4H), 7.18−7.12 (m, 1H), 7.00 (d, J = 8.1 Hz, 1H), 6.95−6.89 (m, 1H), 4.24−4.22 (m, 1H), 2.55−2.13 (m, 6H), 2.03−1.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 196.0, 169.1, 151.5, 140.2, 129.0, 128.4, 128.2, 127.6, 126.5, 125.6, 121.5, 116.5, 116.0, 99.6, 36.4, 33.0, 27.8, 25.2, 20.7; HRMS (ESI) calcd for $C_{21}H_{19}O_3$ $[M + H]^+$ 319.1329, found 319.1324.

Compound ***8j***. Yellow solid: 132 mg, 76% yield; mp 99−100 °C; IR (KBr, cm^{-1}) 3452, 2943, 1625, 1383, 1243, 1176, 1107, 1026, 826, 755; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.58 (d, J = 9.0 Hz, 2H),

7.41−7.38 (m, 1H), 7.17−7.11 (m, 1H), 7.01−6.89 (m, 4H), 4.21 (s, 1H), 3.84 (s, 3H), 2.54−2.31 (m, 4H), 2.26−2.12 (m, 2H), 2.02−1.92 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 196.0, 169.2, 160.1, 151.5, 132.5, 128.1, 127.5, 126.9, 126.6, 121.4, 116.5, 115.9, 113.7, 99.7, 55.3, 36.4, 33.0, 27.8, 25.3, 20.7; HRMS (ESI) calcd for $C_{22}H_{21}O_4$ $[M + H]^+$ 349.1434, found 349.1431.

Compound ***8k***. Yellow solid: 148 mg, 84% yield; mp 162−163 °C; IR (KBr, cm^{-1}) 3443, 1626, 1384, 1236, 1103, 1024, 835, 758; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.60 (d, J = 8.4 Hz, 2H), 7.43−7.40 (m, 3H), 7.18−7.13 (m, 1H), 7.01−6.90 (m, 2H), 4.22 (s, 1H), 2.52−2.15 (m, 6H), 2.02−1.95 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.9, 168.8, 151.3, 138.8, 135.1, 128.6, 128.2, 127.7, 127.1, 126.4, 121.7, 116.6, 115.9, 99.3, 36.4, 32.9, 27.7, 25.1, 20.7; HRMS (ESI) calcd for $C_{21}H_{18}ClO_3$ $[M + H]^+$ 353.0939, found 353.0941.

Compound ***8l***. Yellow solid: 122 mg, 79% yield; mp 193−194 °C; IR (KBr, cm^{-1}) 3444, 1622, 1382, 1339, 1239, 1156, 1109, 1024, 807, 750; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.48−7.47 (m, 1H), 7.39 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.16−7.10 (m, 1H), 6.97−6.89 (m, 2H), 6.68 (d, J = 3.3 Hz, 1H), 6.45 (dd, J_1 = 3.3 Hz, J_2 = 1.8 Hz, 1H), 4.25−4.23 (m, 1H), 2.50−2.30 (m, 6H), 2.00−1.90 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 196.0, 168.6, 151.6, 150.8, 143.0, 128.2, 127.6, 126.3, 121.7, 116.6, 116.0, 110.4, 107.8, 96.0, 36.4, 29.6, 27.7, 24.3, 20.7; HRMS (ESI) calcd for $C_{19}H_{17}O_4$ $[M + H]^+$ 309.1121, found 309.1123.

Compound ***8m***. Yellow solid: 126 mg, 78% yield; mp 149−150 °C; IR (KBr, cm^{-1}) 3443, 1623, 1383, 1227, 1107, 1029, 866, 754, 712; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.41−7.36 (m, 2H), 7.28−7.25 (m, 1H), 7.17−7.11 (m, 1H), 7.05 (dd, J_1 = 4.8 Hz, J_2 = 3.3 Hz, 1H), 6.99−6.89 (m, 2H), 4.24 (s, 1H), 2.51−2.27 (m, 6H), 1.99−1.93 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 195.9, 168.7, 151.1, 143.6, 128.2, 127.6, 126.8, 126.25, 126.18, 125.1, 121.7, 116.5, 116.0, 98.5, 36.4, 33.1, 27.7, 25.2, 20.6; HRMS (ESI) calcd for $C_{19}H_{17}O_3S$ $[M + H]^+$ 325.0893, found 325.0888.

Compound ***8n***. Yellow solid: 90 mg, 70% yield; mp 144−146 °C; IR (KBr, cm^{-1}) 3439, 2946, 1621, 1381, 1255, 1130, 1059, 862, 820, 756; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.33 (d, J = 7.4 Hz, 1H), 7.11−7.05 (m, 1H), 6.87−6.82 (m, 2H), 4.14−4.12 (m, 1H), 2.41−2.26 (m, 4H), 2.10−2.05 (m, 1H), 1.98−1.86 (m, 3H), 1.81 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 196.0, 169.1, 151.3, 128.1, 127.4, 126.5, 121.1, 116.4, 115.7, 99.0, 36.4, 31.0, 27.8, 26.7, 24.8, 20.7; HRMS (ESI) calcd for $C_{16}H_{17}O_3$ $[M + H]^+$ 257.1172, found 257.1174.

General Procedure for the Synthesis of 10. A mixture of 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one derivatives (**5**, 0.5 mmol) and 2-hydroxynaphthalene-1,4-dione (**9**, 0.5 mmol) was heated at reflux in anhydrous *n*-PrOH in a sealed tube (4.0 mL). After the reactant disappeared (6−12 h, monitored by thin layer chromatography), the mixture was cooled to room temperature and stood overnight. Thus the crystals were precipitated, filtrated and washed with a small amount of anhydrous ethanol, and the target products **10** were obtained as the yellow solids.

Compound ***10a***. Yellow solid: 167 mg, 88% yield; mp 184−185 °C; IR (KBr, cm^{-1}) 3442, 1663, 1642, 1592, 1335, 1241, 1105, 957, 761; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.10−8.07 (m, 2H), 7.77−7.67 (m, 4H), 7.51−7.44 (m, 4H), 7.21−7.16 (m, 1H), 7.06−6.93 (m, 2H), 4.56 (t, J = 2.8 Hz, 1H), 2.46 (dd, J_1 = 13.6 Hz, J_2 = 2.8 Hz, 1H), 2.30 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.7, 178.8, 153.2, 151.8, 139.4, 134.0, 133.4, 131.7, 131.0, 129.3, 128.54, 128.47, 128.4, 126.5, 126.2, 125.8, 124.7, 124.2, 121.9, 116.6, 100.1, 32.1, 26.2; HRMS (ESI) calcd for $C_{25}H_{16}O_4Na$ $[M + Na]^+$ 403.0941, found 403.0924.

Compound ***10b***. Yellow solid: 152 mg, 74% yield; mp 189−190 °C; IR (KBr, cm^{-1}) 3440, 1684, 1623, 1593, 1512, 1336, 1165, 1097, 946, 884, 756; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.08−8.05 (m, 2H), 7.71−7.66 (m, 4H), 7.47−7.44 (m, 1H), 7.17−7.14 (m, 1H), 7.04−6.92 (m, 4H), 4.53 (s, 1H), 3.85 (s, 3H), 2.44 (dd, J_1 = 13.6 Hz, J_2 = 3.0 Hz, 1H), 2.29 (dd, J_1 = 13.6 Hz, J_2 = 3.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.7, 178.8, 160.2, 153.2, 151.8, 134.0, 133.3, 131.7, 131.6, 130.9, 128.4, 128.3, 127.1, 126.4, 126.1, 124.6, 124.2, 121.8, 116.6, 113.8, 100.1, 55.3, 32.1, 26.2; HRMS (ESI) calcd for $C_{26}H_{18}O_5Na$ $[M + Na]^+$ 433.1046, found 433.1038.

Compound ***10c***. Yellow solid: 156 mg, 71% yield; mp 185−186 °C; IR (KBr, cm^{-1}) 3441, 1678, 1637, 1595, 1522, 1337, 1243, 1132, 1033, 952, 896, 756; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.10−8.07 (m, 2H), 7.73−7.67 (m, 2H), 7.46 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.33−7.28 (m, 2H), 7.21−7.16 (m, 1H), 7.06−6.93 (m, 3H), 4.56−4.54 (m, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 2.48 (dd, J_1 = 13.6 Hz, J_2 = 2.8 Hz, 1H), 2.29 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.7, 178.8, 153.2, 151.8, 149.7, 148.8, 134.0, 133.4, 131.9, 131.7, 130.9, 128.5, 128.4, 126.4, 126.2, 124.7, 124.1, 121.9, 118.4, 116.6, 110.8, 109.1, 100.0, 55.99, 55.97, 32.0, 26.2; HRMS (ESI) calcd for $C_{27}H_{20}O_6Na$ $[M + Na]^+$ 463.1152, found 463.1130.

Compound ***10d***. Yellow solid: 170 mg, 82% yield; mp 218−219 °C; IR (KBr, cm^{-1}) 3424, 3066, 1686, 1635, 1591, 1485, 1403, 1336, 1242, 1096, 1007, 951, 886, 761; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.08 (d, J = 6.8 Hz, 2H), 7.69 (d, J = 8.1 Hz, 4H), 7.48−7.43 (m, 3H), 7.21−7.16 (m, 1H), 7.05−6.94 (m, 2H), 4.55 (s, 1H), 2.45−2.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.6, 178.7, 153.0, 151.6, 138.0, 135.4, 134.1, 133.5, 131.6, 130.9, 128.7, 128.5, 127.3, 126.5, 126.2, 124.7, 124.0, 122.1, 116.6, 99.6, 32.0, 26.1; HRMS (ESI) calcd for $C_{25}H_{15}ClO_4Na$ $[M + Na]^+$ 437.0551, found 437.0533.

Compound ***10e***. Yellow solid: 183 mg, 80% yield; mp 234−235 °C; IR (KBr, cm^{-1}) 3440, 1684, 1626, 1590, 1482, 1336, 1241, 1098, 1005, 951, 886, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.11−8.07 (m, 2H), 7.75−7.58 (m, 6H), 7.48−7.45 (m, 1H), 7.22−7.16 (m, 1H), 7.05−6.94 (m, 2H), 4.55 (t, J = 2.9 Hz, 1H), 2.43 (dd, J_1 = 13.6 Hz, J_2 = 2.8 Hz, 1H), 2.27 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.6, 178.7, 152.9, 151.6, 138.5, 134.1, 133.5, 131.7, 131.6, 130.9, 128.50, 128.49, 127.6, 126.5, 126.2, 124.7, 124.0, 123.6, 122.1, 116.6, 99.7, 31.9, 26.1; HRMS (ESI) calcd for $C_{25}H_{15}BrO_4Na$ $[M + Na]^+$ 481.0046, found 481.0021.

Compound ***10f***. Yellow solid: 169 mg, 85% yield; mp 188−189 °C; IR (KBr, cm^{-1}) 3439, 1661, 1639, 1623, 1592, 1514, 1335, 1236, 1158, 1098, 1021, 947, 832, 758; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.10−8.08 (m, 2H), 7.76−7.67 (m, 4H), 7.48−7.45 (m, 1H), 7.21−7.13 (m, 3H), 7.05−6.94 (m, 2H), 4.55 (t, J = 2.7 Hz, 1H), 2.44 (dd, J_1 = 13.6 Hz, J_2 = 2.7 Hz, 1H), 2.28 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.7, 178.8, 163.2 (d, $^1J_{CF}$ = 246.8 Hz), 153.0, 151.7, 135.4 (d, $^4J_{CF}$ = 3.2 Hz), 134.1, 133.5, 131.7, 131.0, 128.5, 128.4, 127.9 (d, $^3J_{CF}$ = 8.5 Hz), 126.5, 126.2, 124.7, 124.0, 122.1, 116.6, 115.5 (d, $^2J_{CF}$ = 21.6 Hz), 99.7, 32.1, 26.2; HRMS (ESI) calcd for $C_{25}H_{15}FO_4Na$ $[M + Na]^+$ 421.0847, found 421.0868.

Compound ***10g***. Yellow solid: 133 mg, 72% yield; mp 191−192 °C; IR (KBr, cm^{-1}) 3442, 1662, 1642, 1625, 1591, 1333, 1240, 1161, 1104, 957, 716; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.08−8.05 (m, 2H), 7.69−7.65 (m, 2H), 7.49−7.44 (m, 2H), 7.16−7.13 (m, 1H), 7.01−6.92 (m, 2H), 6.85−6.83 (m, 1H), 6.48 (dd, J_1 = 3.3 Hz, J_2 = 1.8 Hz, 1H), 4.56 (t, J = 2.9 Hz, 1H), 2.56 (dd, J_1 = 13.5 Hz, J_2 = 2.8 Hz, 1H), 2.48 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.6, 178.5, 152.7, 151.2, 150.5, 143.3, 134.0, 133.4, 131.6, 130.9, 128.5, 128.4, 126.5, 126.2, 124.6, 124.0, 122.1, 116.6, 110.6, 108.7, 96.5, 28.8, 25.3; HRMS (ESI) calcd for $C_{23}H_{14}O_5Na$ $[M + Na]^+$ 393.0733, found 393.0721.

Compound ***10h***. Yellow solid: 135 mg, 70% yield; mp 193−194 °C; IR (KBr, cm^{-1}) 3441, 1662, 1623, 1589, 1326, 1235, 1197, 1098, 951, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.08 (d, J = 5.8 Hz, 2H), 7.69 (s, 2H), 7.47−7.39 (m, 3H), 7.19−6.94 (m, 4H), 4.57 (s, 1H), 2.61−2.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.7, 178.5, 152.8, 151.4, 142.4, 134.0, 133.5, 131.6, 130.9, 128.5, 128.4, 127.0, 126.6, 126.5, 126.2, 125.7, 124.6, 123.9, 122.1, 116.7, 99.0, 32.3, 26.2; HRMS (ESI) calcd for $C_{23}H_{14}O_4SNa$ $[M + Na]^+$ 409.0505, found 409.0492.

Compound ***10i***. Yellow solid: 108 mg, 68% yield; mp 220−221 °C; IR (KBr, cm^{-1}) 3441, 1660, 1622, 1588, 1337, 1257, 1213, 1145, 1098, 942, 866, 767; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.06−8.02 (m, 2H), 7.70−7.63 (m, 2H), 7.41−7.38 (m, 1H), 7.14−7.11 (m, 1H), 7.09−6.86 (m, 2H), 4.56 (t, J = 2.8 Hz, 1H), 2.28 (dd, J_1 = 13.6 Hz, J_2 = 2.8 Hz, 1H), 2.14 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H), 1.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.7, 179.0, 153.0, 151.6,

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134.0, 133.3, 131.6, 130.9, 128.3, 128.2, 126.4, 126.1, 124.5, 124.1, 121.5, 116.3, 99.7, 30.1, 26.5, 25.8; HRMS (ESI) calcd for $C_{20}H_{14}O_4Na$ $[M + Na]^+$ 341.0784, found 341.0774.

Compound ***10j***. Yellow solid: 170 mg, 82% yield; mp 211−212 °C; IR (KBr, cm^{-1}) 3439, 1663, 1624, 1590, 1478, 1333, 1243, 1199, 1097, 953, 760; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.11−8.08 (m, 2H), 7.75−7.69 (m, 4H), 7.50−7.45 (m, 4H), 7.15−7.11 (m, 1H), 6.97 (d, J = 8.7 Hz, 1H), 4.51 (t, J = 2.6 Hz, 1H), 2.43 (dd, J_1 = 13.7 Hz, J_2 = 2.6 Hz, 1H), 2.30 (dd, J_1 = 13.6 Hz, J_2 = 3.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.5, 178.6, 153.2, 150.4, 138.9, 134.2, 133.5, 131.6, 130.9, 129.4, 128.6, 128.4, 128.1, 126.7, 126.5, 126.3, 125.7, 124.1, 117.9, 100.1, 31.7, 26.0; HRMS (ESI) calcd for $C_{25}H_{15}ClO_4Na$ $[M + Na]^+$ 437.0551, found 437.0537.

Compound ***10k***. Yellow solid: 186 mg, 83% yield; mp 208−209 °C; IR (KBr, cm^{-1}) 3442, 1639, 1452, 1348, 1252, 1200, 1096, 928, 708; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.13−8.09 (m, 2H), 7.79−7.71 (m, 4H), 7.50−7.26 (m, 5H), 4.51 (t, J = 2.8 Hz, 1H), 2.43−2.31 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.4, 178.4, 153.1, 146.6, 138.3, 134.2, 133.7, 131.5, 130.9, 129.6, 128.8, 128.7, 127.1, 126.7, 126.6, 126.5, 126.3, 125.9, 123.3, 122.5, 100.5, 31.7, 26.3; HRMS (ESI) calcd for $C_{25}H_{14}Cl_2O_4Na$ $[M + Na]^+$ 471.0161, found 471.0148.

Compound ***10l***. Yellow solid: 179 mg, 78% yield; mp 205−206 °C; IR (KBr, cm^{-1}) 3440, 1663, 1637, 1589, 1477, 1332, 1243, 1198, 1100, 953, 759; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.09 (d, J = 7.0 Hz, 2H), 7.73−7.60 (m, 4H), 7.48−7.46 (m 4H), 7.29−7.25 (m, 1H), 6.92 (d, J = 8.7 Hz, 1H), 4.51 (s, 1H), 2.45−2.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.5, 178.6, 153.1, 151.0, 138.9, 134.2, 133.5, 131.6, 131.3, 130.9, 129.4, 128.6, 126.5, 126.3, 126.2, 125.7, 124.1, 118.3, 114.1, 100.0, 31.7, 26.0; HRMS (ESI) calcd for $C_{25}H_{15}BrO_4Na$ $[M + Na]^+$ 481.0046, found 481.0046.

Synthesis of 3-(2-Phenyl-4*H*-chromen-4-yl)pentane-2,4-dione (12). A mixture of 3-(2-hydroxyphenyl)-1-phenylprop-2-en-1-one (**5a**, 224 mg, 1.0 mmol) and pentane-2,4-dione (**11**, 100 mg, 1.0 mmol) was heated at reflux in anhydrous toluene in a sealed tube (6.0 mL). After the reactant disappeared (10 h, monitored by thin layer chromatography), the mixture was cooled to room temperature and directly added to the column chromatography using petroleum ether as the eluent to remove toluene, then eluting with petroleum ether/ethyl acetate to give the product **12** as a yellow solid: 217 mg, 71% yield; mp 100−101 °C; IR (KBr, cm^{-1}) 3443, 2359, 1631, 1390, 1121, 476; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.67−7.64 (m, 2H), 7.42−7.35 (m, 3H), 7.28−7.22 (m, 1H), 7.14−7.03 (m, 3H), 5.61 (d, J = 5.4 Hz, 1H), 7.05 (dd, J_1 = 7.6 Hz, J_2 = 5.4 Hz, 1H), 4.10 (d, J = 7.6 Hz, 1H), 2.12 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 203.1, 202.4, 152.5, 151.1, 133.6, 128.9, 128.37, 128.35, 128.32, 124.8, 123.9, 121.3, 117.0, 97.8, 75.3, 35.1, 31.7, 31.0; HRMS (ESI) calcd for $C_{20}H_{18}O_3Na$ $[M + Na]^+$ 329.1148, found 329.1144.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H, ^{13}C NMR spectra for the products and CIF files of **6a** and **8f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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