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HFIP Promoted C3-Alkylation of Lawsone and 4-Hydroxycoumarin with Alcohols by Dehydrative Cross-Coupling

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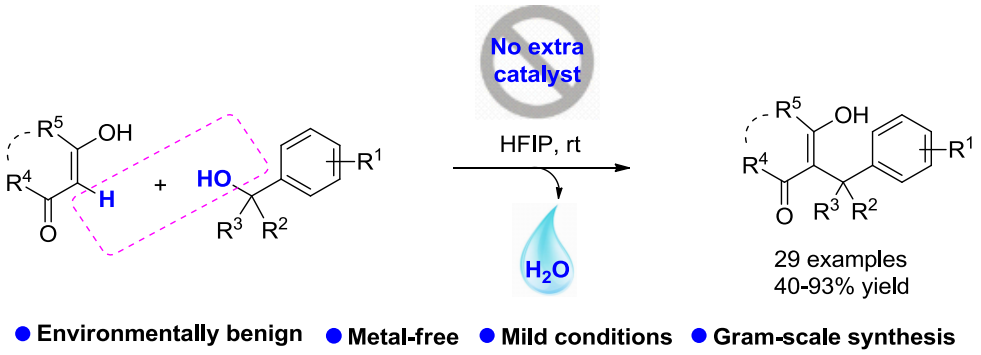
Graphical Abstract



ABSTRACT

An environmentally benign system for the direct alkylation of lawsones and 4-hydroxycoumarins with alcohols in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) is reported. The reaction proceeded smoothly via a dehydrative cross-coupling process by utilizing the unique properties of HFIP. A variety of alkylated products and subsequent one-pot cyclized products (pyranonaphthoquinones and pyranocoumarins) could be obtained in 40–93% yields.

INTRODUCTION

C3-Alkylated lawsones are valuable structural motifs which have wide range application in natural products and pharmaceutical industry due to their unique biological properties such as

antibacterial, antifungal, anticancer, antiviral, and antiprotozoal activities.[1] Examples include lapachol, dunniol, atovaquone, buparvaquone, streptocarpone, α-lapachone and α-dunnione (Figure 1).[2] These comprehensive bioactivity profiles and drug-like characteristics have attracted extensive attention from pharmacologists and synthetic organic chemists. As a consequence, great efforts have been made to develop various methods for regioselective synthesis of C3-alkylated lawsones in the past decades.[3] Among existing methods for synthesizing C3-substituted lawsone derivatives, the C–C bond forming reactions between lawsone and different alkylating agents would represent one of the most straightforward synthetic methods. The traditional alkylation of lawsone with alkyl halides in the presence of a stoichiometric amount of base usually gives a mixture of C- and O-alkylated products with low yields and regioselectivities (Scheme 1 A).[4] Silver-mediated alkylation of lawsone using carboxylic acids or peroxides provides an alternative, but harsh reaction conditions limit its scope (Scheme 1 B).[5] Recently, Cheng and co-workers reported a DDQ-promoted cross-dehydrogenative coupling reaction between lawsone and 1,3-diarylpropene for the synthesis of C3-alkylated lawsone (Scheme 1 C).[6] However, the use of a stoichiometric amount of DDQ often generates large quantities of hydroquinone as by-product, which makes purification process difficult.

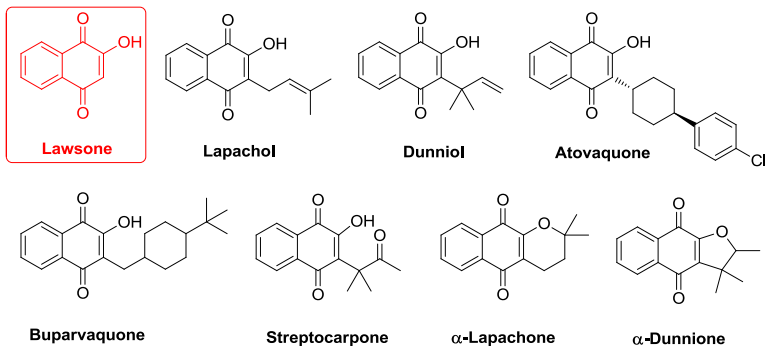
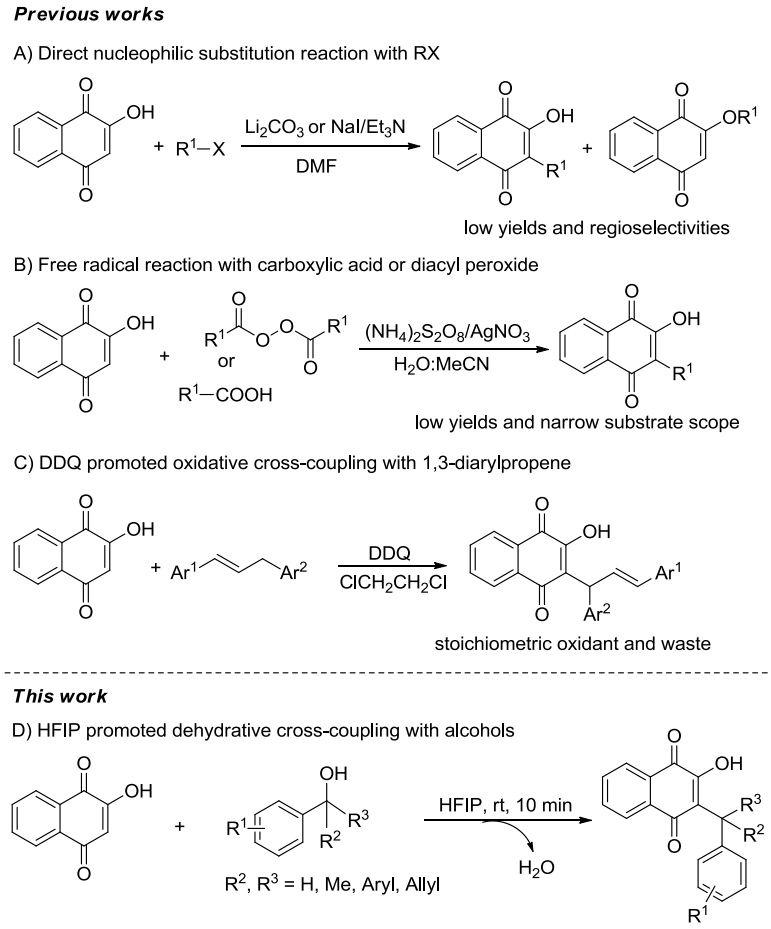


Figure 1. Representative biologically active natural molecules and drugs containing C3-alkylated lawsone moieties.

Scheme 1. Different C3-Alkylation Strategies of Lawsones.



Taking hazardous waste minimization and environmental sustainability into account, the metal-free direct substitution of alcohols via dehydrative cross-coupling is highly desired and represents a much ecologically benign, step- and atom-economical approach with water as the only by-product.[7] However, the reactions using the corresponding alcohols have not been well studied. Only in rare cases, palladium catalyst and high temperature environment were demanded to promote the benzylation and allylation of lawsone with specific alcohol or its acetate, which was probably due to the high activation barrier for C–OH scission (85−91 kcal mol^{-1}).[8] In this regard, a catalyst-free and milder methodology for the C3-alkylation of lawsone is worthy to explore. Fluorinated alcohols may be considered as a promising alternative to address this synthetic challenge due to their unique properties such as high polarity, high H-bond donor ability,

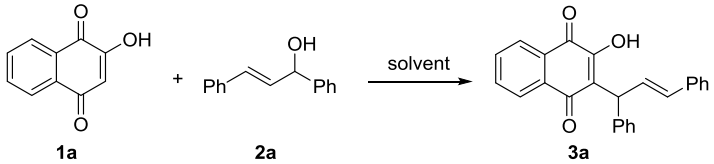
high dielectric constant and low nucleophilicity for cation stabilization.[9] The above properties of fluorinated alcohols would provide the possibility of performing this dehydrative cross-coupling reaction using alcohols in a user-friendly and environmentally friendly transformation (Scheme 1 D).

RESULTS AND DISCUSSION

The alkylation of lawsone **1a** with 1,3-diarylpropenol (chalcol) **2a** was selected as the model reaction for the reaction condition optimization. We first examined the reaction in pure 2,2,2-trifluoroethanol (TFE) solvent, and the reaction mixture was stirred at room temperature under air. To our delight, C3-alkylated lawsone **3a** was obtained in 68% yield with excellent regioselectivity (Table 1, entry 1). Another fluorinated solvent with a much stronger polarity, ionizing power, Brønsted acidity, and hydrogen-bonding ability, 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), was then tested. Unexpectedly, the transformation proceeded rapidly to afford the desired product in 87% yield in 10 minutes (entry 2). Other nonfluorinated alcohols, such as isopropanol and ethanol, as well as water with high polarity and hydrogen bonding capability were selected as the solvents, none of the desired product was obtained with the formation of unwanted etherified or dimerizated product of chalcol **2a** (entries 3–5). No product was detected when perfluorohexane was used as solvent, which indicating that fluorine atom is not the sole factor promoting the reaction smoothly (entry 6). The employment of weak acidic media to produce C3-alkylated lawsone was unsuccessful (entry 7). When HFIP was used as a mixed solvent, the yields of the expected product decreased greatly (entries 8–11). Regulating the reaction temperature did not result in any further improvement in yields. Thus, the optimal condition is that the reaction was stirred in HFIP at room temperature without any extra

catalyst.

Table 1 Optimization of the Reaction Conditions for the C3-Alkylation of Lawsone with Chalcol[a]



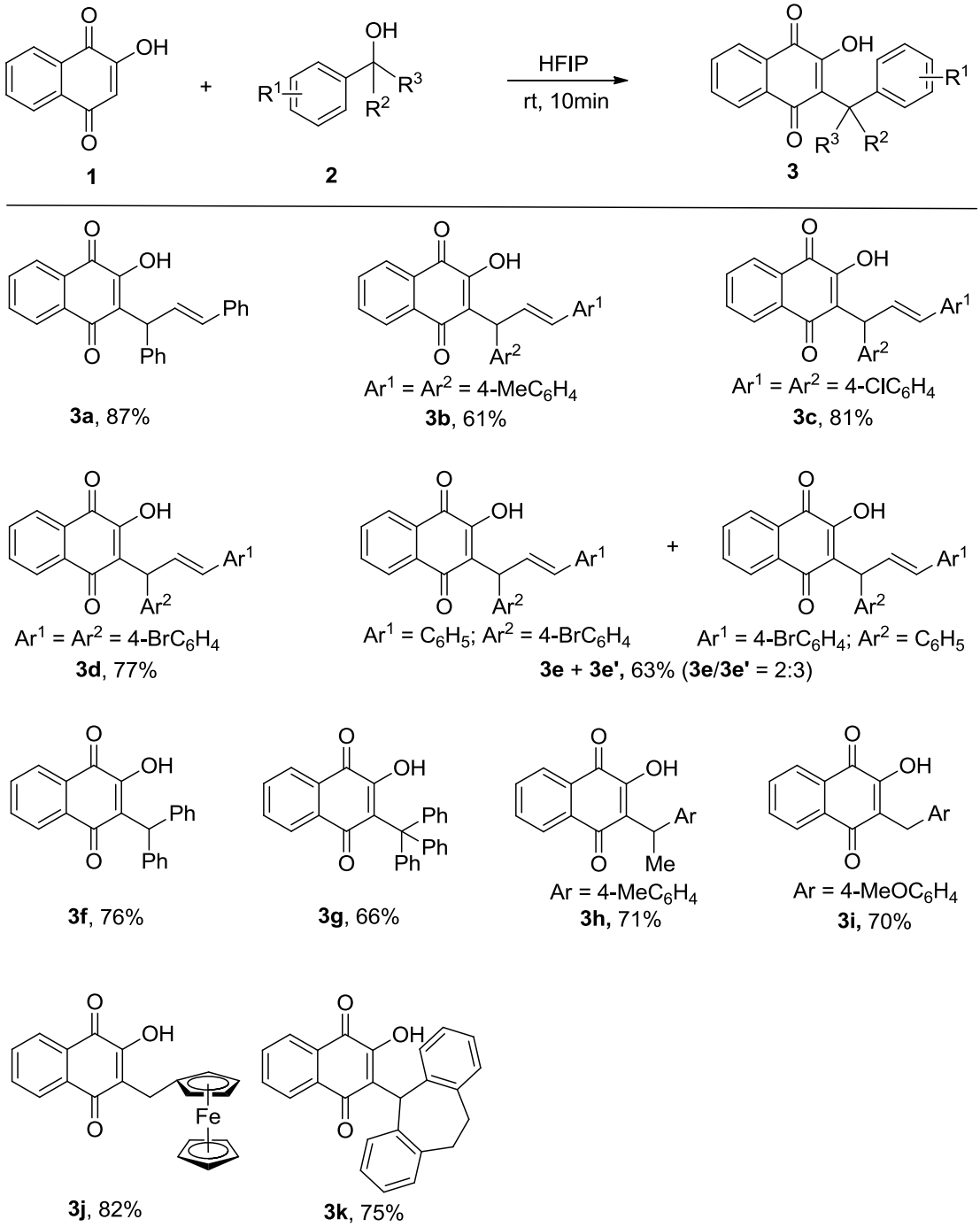
entry	solvent	Time (h)	yield (%)[b]
1	TFE[c]	1	68
2	HFIP[d]	10 min	87
3	^{i}PrOH	12	trace
4	EtOH	12	0
5	H_2O	12	0
6	C_6F_{14}[e]	12	0
7	$CHCl_3$	12	0
8	HFIP/ $CHCl_3$ = 1:1	12	38
9	HFIP/ ^{i}PrOH = 1:1	12	52
10	HFIP/ EtOH = 1:1	12	55
11	HFIP/ H_2O = 1:1	12	45

[a]Reaction conditions: **1a** (1.2 mmol), **2a** (1.0 mmol) in solvent (5.0 mL) at room temperature unless otherwise noted. [b]Isolated yields. [c]TFE = 2,2,2-trifluoroethanol. [d]HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol. [e]C_6F_{14} = perfluorohexane.

With the optimized reaction conditions established for this dehydrative cross-coupling reaction, we embarked on the investigation of substrate scope to probe the generality of the reaction. A series of alcohols **2** were treated with lawsone **1** to form the alkylated products in HFIP at ambient temperature (Scheme 2). Chalcols bearing electron-donating or electron-withdrawing groups on the aromatic ring all functioned well in the C3-alkylation of lawsone, affording the desired product in 61–87% yields (**3a**-**3e**). It should be pointed out that both isomers were detected when the asymmetrical chalcol **2e** was employed, giving the corresponding inseparable products (**3e**/**3e'** = 2:3) in 63% yield. According to forecasting results, it indicates that allyl cations was formed and rearranged occurred between α- and γ-positions during the reaction. In order to evaluate the scope and limitations of this methodology, a range of benzyl alcohols were converted under the optimal

reaction conditions developed for the alkylation of lawsone. Primary, secondary and even sterically-hindered tertiary benzylic alcohols could react smoothly with lawsone to furnish the corresponding alkylated products in 66–82% yields (**3f**-**3k**).

Scheme 2. Dehydrative Cross-Coupling of Lawsones with Alcohols in HFIP.[a,b]



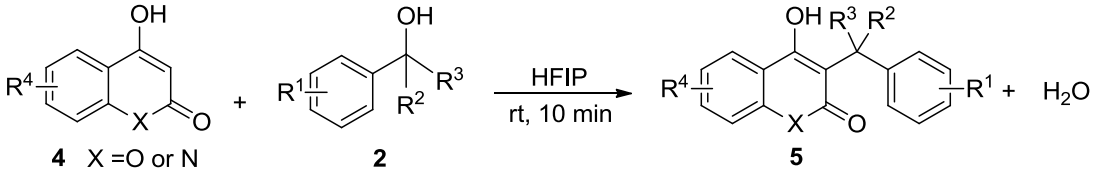
[a]Reaction conditions: **1** (1.2 mmol), **2** (1.0 mmol) in HFIP (5.0 mL) at room temperature. [b]Isolated yields based on **2**.

C3-Alkylated coumarins are one of the most important classes of heterocyclic compounds and known to exhibit a wide spectrum of pharmacological properties including antibiotic, antifungal, anticoagulant activities.[10] A great number of methods have been developed for the C3-alkylation of 4-hydroxycoumarins by using alcohols with Lewis acids, such as TMSOTf, $BF_3 \cdot Et_2O$, Amberlyst IR-120, $Bi(OTf)_3$, $Yb(OTf)_3$, I_2, Pd-Sn bimetallic system or microwave.[11] However, high toxicity, corrosion, catalyst waste problems are almost inevitable in these reported processes. To provide a greener and more efficient method for the alkylation of 4-hydroxycoumarin through dehydrative cross-coupling strategy, the reaction of 4-hydroxycoumarin **4** and alcohols **2** promoted by HFIP was studied. Various desired dehydrative coupling products were obtained in 57–93% yields under the previous optimized reaction conditions (Scheme 3, **5a**-**5o**). 4-Hydroxy-2-quinolinone **2p** was also a viable substrate for the reaction. The corresponding product **5p** was obtained in 40% yield. More interestingly when the hydroxyl group on the 4-hydroxycoumarin was replaced by an amino group, product **5q** was obtained in 90% yield. In addition, it was further found that 3-alkylated 4-hydroxycoumarins related natural products or drugs, such as Phenprocoumon **5r** and Coumatetarlyl **5s** could be obtained on a 5.0 mmol scale from lawsone and 4-hydroxycoumarin upon reaction with corresponding alcohols. Moreover, Stiripentol, used as an anticonvulsant drug in the treatment of pediatric epilepsy, can be easily functionalized with 4-hydroxycoumarin by using our newly developed methodology on a gram scale.

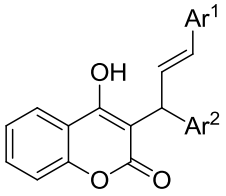
To demonstrate the synthetic utility of this protocol, we conducted further manipulation by utilizing the sequential dehydrative cross-coupling/cyclization reactions with lawsone for the synthesis of pyranonaphthoquinones in a one-pot manner (Scheme 4). This consecutive

transformation displays the synthetic potential of the developed procedure. The cyclized product **6a** was smoothly obtained in 78% yield with the addition of one equivalent of DDQ into the reaction mixture after the alkylation reaction of lawsone **1a** with chalcol **2a** finished. Various pyranonaphthoquinones and pyranocoumarins were provided in 49–80% yields.

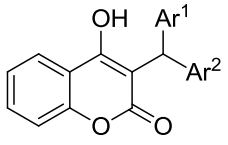
Scheme 3. Dehydrative Cross-Coupling of 4-Hydroxycoumarins with Alcohols in HFIP.[a,b]



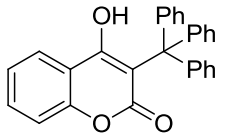
4 X =O or N **2** **5**



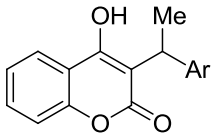
5a, $Ar^1 = Ar^2 = C_6H_5$, 93%
5b, $Ar^1 = Ar^2 = 3\text{-}MeC_6H_4$, 77%
5c, $Ar^1 = Ar^2 = 4\text{-}MeC_6H_4$, 69%
5d, $Ar^1 = Ar^2 = 4\text{-}ClC_6H_4$, 83%
5e, $Ar^1 = Ar^2 = 4\text{-}BrC_6H_4$, 87%



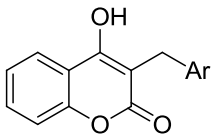
5f, $Ar^1 = Ar^2 = C_6H_5$, 80%
5g, $Ar^1 = Ar^2 = 4\text{-}FC_6H_4$, 87%
5h, $Ar^1 = Ar^2 = 4\text{-}ClC_6H_4$, 88%



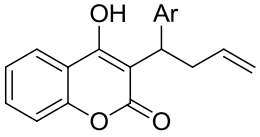
5i, 71%



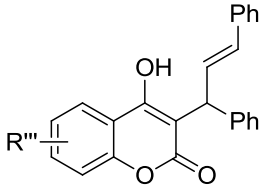
5j, Ar = $4\text{-}MeC_6H_4$, 69%



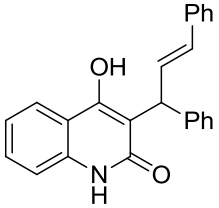
5k, Ar = $4\text{-}MeOC_6H_4$, 78%



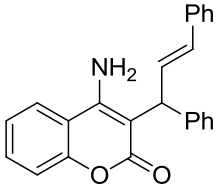
5l, Ar = $4\text{-}MeC_6H_4$, 57%



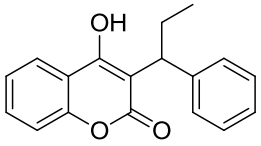
5m, R''' = 6-Me, 86%
5n, R''' = 6-F, 74%
5o, R''' = 6-Br, 78%



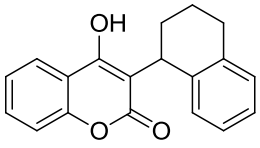
5p, 40%



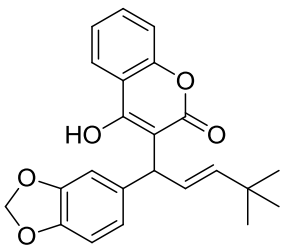
5q, 90%



Phenprocoumon, 5r
5.0 mmol, 757 mg, 54%



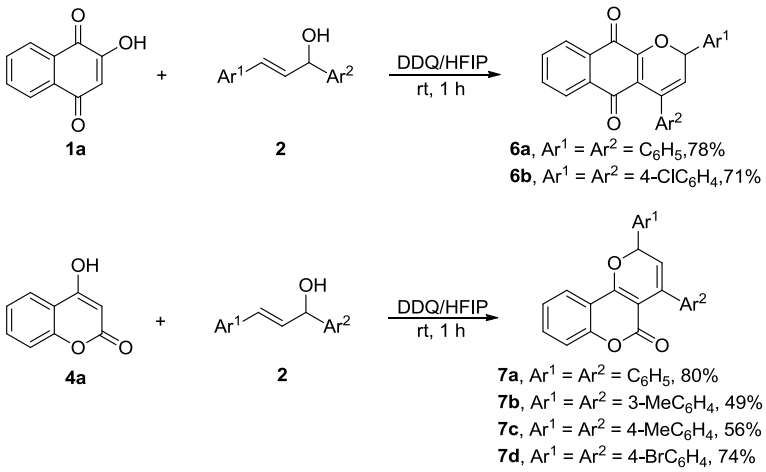
Coumatetarlyl, 5s
5.0 mmol, 950 mg, 65%



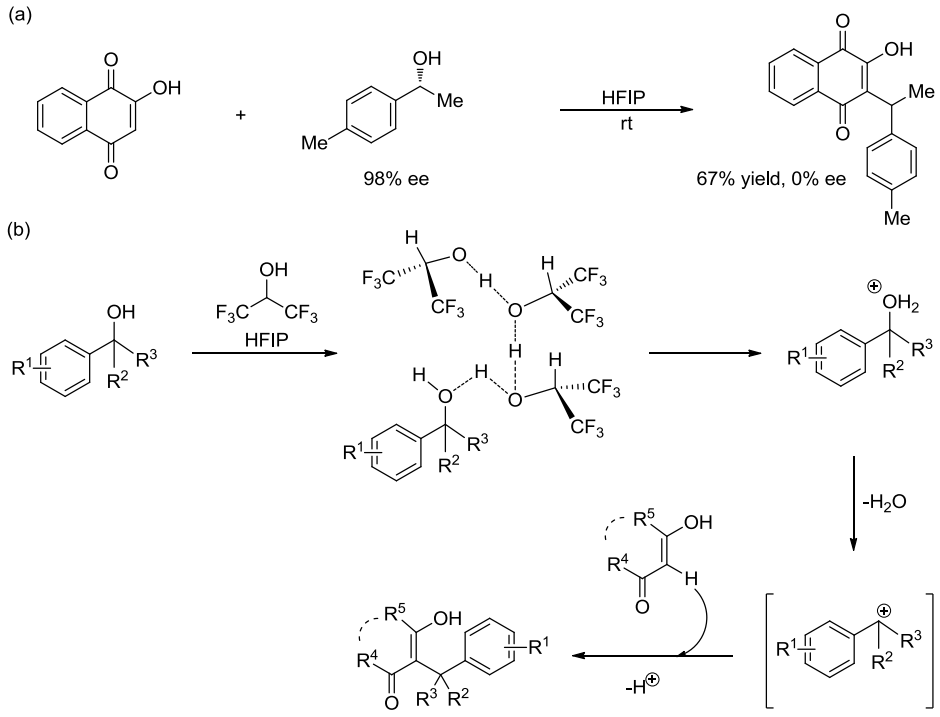
From Stiripentol, 5t
5.0 mmol, 1.47 g, 78%

[a]Reaction conditions: **4** (1.2 mmol), **2** (1.0 mmol) in HFIP (5.0 mL) at room temperature. [b]Isolated yields based on **2**.

Scheme 4. One-Pot Sequential Dehydrative Cross-Coupling and Cyclization Reaction for the Syntheses of Pyranonaphthoquinones and Pyranocoumarins.



Scheme 5. Plausible mechanism.



On the basis of results of dehydrative cross-coupling of lawsone with chiral alcohol (Scheme 5a, 98% ee) and previous studies[16], a S_N1 mechanism was proposed in Scheme 5b. The alcohol is protonated by HFIP to give an oxonium ion via hydrogen bonding interaction. Then oxonium ion

is dehydrated to form a stabilized carbocation intermediate, which is attacked by the nucleophilic reagent lawsone or 4-hydroxycoumarin to give the coupling products.

CONCLUSIONS

In summary, a HFIP-promoted dehydrative cross-coupling reaction between lawsones, 4-hydroxycoumarin and alcohols has been developed. The use of alcohols as alkylating agents avoided the need for pre-activation treatment and water was the sole byproduct utilizing this method, which would be a more environmentally benign way than existing protocols. In addition, a series of C3-alkylated lawsone and 4-hydroxycoumarin derivatives with potential bioactivities could be easily synthesized with the developed approach.

EXPERIMENTAL SECTION

General Information. ^{1}H, ^{13}C and ^{19}F were recorded on Bruker AV 400 MHz instrument at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR), as well as 376 MHz (^{19}F NMR). Chemical shifts were reported in ppm down field from internal Me_4Si and external CCl_3F, respectively. $CDCl_3$ (7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR), or DMSO-d_6 (2.50 ppm for ^{1}H NMR, 39.5 ppm for ^{13}C NMR) was used as a reference. Data for ^{1}H were reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, br = broad singlet), coupling constants (Hz), and integration. Data for ^{13}C NMR were reported as ppm. High-resolution mass spectra analyses were performed on a Waters SYNAPT G2-Si Q-TOF mass spectrometer. Melting points were determined using a X-4 digital micro melting point apparatus. Thin-layer chromatography (TLC) was performed, and visualization of the compounds was accomplished with UV light (254 nm). Flash column chromatography was performed on silica gel (200−300 mesh). Chalcols **2a**−**2e** and alcohol **2l** were prepared according

to literature procedures.[12] Purchased reagents and solvents were used without further purification.

General Procedure for Preparation of 3-Alkylated Lawsones 3. A mixture of the substrate **1** (1.2 mmol), substrate **2** (1.0 mmol), in HFIP (5.0 mL) was stirred at room temperature for 10 min. Upon completion of the reaction, the resulting mixture was and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 8:1) to give the pure product **3**; the method is also suitable for the alkylation of 4-hydroxycoumarins **4**.

(*E*)-2-(1,3-Diphenylallyl)-3-hydroxynaphthalene-1,4-dione (3a): orange oil (318 mg, 87% yield, hexane/EtOAc = 8/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 7.7 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.81 (t, J = 7.5 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 7.47 (d, J = 7.6 Hz, 4H), 7.35 (t, J = 7.5 Hz, 4H), 7.30 (s, 1H), 7.26 (t, J = 7.2 Hz, 2H), 7.06 (dd, J = 15.8, 8.9 Hz, 1H), 6.67 (d, J = 15.8 Hz, 1H), 5.44 (d, J = 8.9 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.8, 181.9, 152.8, 141.7, 137.3, 135.2, 133.1, 132.9, 132.5, 129.3, 128.6, 128.6, 128.4, 127.8, 127.5, 127.2, 126.5, 126.5, 126.2, 124.8, 44.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{18}O_3Na$ 389.1154; Found 389.1153. Physical and spectral properties of this material were identical to those previously reported in literature.[6]

(*E*)-2-(1,3-Di-*p*-tolylallyl)-3-hydroxynaphthalene-1,4-dione (3b): orange oil (240 mg, 61% yield, hexane/EtOAc = 8/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, J = 24.1, 7.3 Hz, 2H), 7.64 (td, J = 7.6, 1.3 Hz, 1H), 7.56 (td, J = 7.5, 1.2 Hz, 1H), 7.47 (s, 1H), 7.22 (d, J = 7.8 Hz, 4H), 7.01 (d, J = 7.5 Hz, 4H), 6.85 (dd, J = 15.3, 9.3 Hz, 1H), 6.48 (d, J = 15.8 Hz, 1H), 5.25 (d, J = 8.9 Hz, 1H), 2.21 (d, J = 5.4 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.9, 152.7, 138.8, 137.2, 136.0, 135.13, 134.5, 133.0, 132.9, 132.2, 129.1, 127.7, 127.1, 126.3, 126.1, 125.1, 43.7, 21.2, 21.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{27}H_{22}O_3Na$ 417.1467; Found 417.1469.

(*E*)-2-(1,3-Bis(4-chlorophenyl)allyl)-3-hydroxynaphthalene-1,4-dione (3c): orange oil (351 mg, 81% yield, hexane/EtOAc = 7/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 12.7, 8.1 Hz, 2H), 7.78 (t, J = 7.6 Hz, 1H), 7.70 (t, J = 7.5 Hz, 1H), 7.41 (dd, J = 8.5, 3.9 Hz, 4H), 7.27 (d, J = 7.1 Hz, 5H), 6.92 (dd, J = 15.8, 8.8 Hz, 1H), 6.53 (d, J = 15.8 Hz, 1H), 5.30 (d, J = 8.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.7, 181.6, 152.9, 140.5, 136.0, 135.3, 133.2, 132.7, 131.7, 131.5, 129.6, 129.2, 128.8, 128.0, 127.2, 126.3, 124.0, 121.4, 120.5, 43.6; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{16}Cl_2O_3Na$ 457.0374; Found 457.0371.

(*E*)-2-(1,3-Bis(4-bromophenyl)allyl)-3-hydroxynaphthalene-1,4-dione (3d): orange oil (402 mg, 77% yield, hexane/EtOAc = 7/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 13.4, 7.6 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.57 (s, 1H), 7.41 (dd, J = 8.5, 2.7 Hz, 4H), 7.28 (d, J = 3.0 Hz, 2H), 6.92 (dd, J = 15.8, 8.8 Hz, 1H), 6.53 (d, J = 15.8 Hz, 1H), 5.29 (d, J = 8.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.7, 181.6, 152.9, 140.5, 136.0, 135.3, 132.7, 131.7, 131.5, 129.6, 129.2, 128.9, 128.0, 127.2, 126.3, 121.4, 120.5; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{16}Br_2O_3Na$ 546.9343; Found 546.9348.

Mixture of (*E*)-2-(1-(4-Bromophenyl)-3-phenylallyl)-3-hydroxynaphthalene-1,4-dione and (*E*)-2-(3-(4-Bromophenyl)-1-phenylallyl)-3-hydroxynaphthalene-1,4-dione (2:3) (3e and 3e'): orange oil (280 mg, 63% yield, hexane/EtOAc = 7/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (dd, J = 16.7, 7.6 Hz, 2H), 7.72 (dt, J = 31.9, 7.6 Hz, 2H), 7.54 (s, 1H), 7.41 (dd, J = 8.6, 2.2 Hz, 4H), 7.33 – 7.25 (m, 5H), 7.22 (d, J = 7.1 Hz, 1H), 7.06 – 6.86 (m, 1H), 6.57 (dd, J = 27.3, 15.7 Hz, 1H), 5.34 (dd, J = 19.4, 8.9 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.8, 152.8, 141.4, 136.2, 135.2, 133.1, 132.9, 131.6, 131.4, 131.2, 129.6, 128.6, 128.5, 128.0, 127.8, 127.2, 126.6, 126.2, 44.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{17}BrO_3Na$ 467.0259; Found

467.0265. Physical and spectral properties of this material were identical to those previously reported in literature.[6]

2-Benzhydryl-3-hydroxynaphthalene-1,4-dione (3f): orange oil (258 mg, 76% yield, hexane/EtOAc = 8/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, J = 20.0, 7.7 Hz, 2H), 7.76 (td, J = 7.6, 1.4 Hz, 1H), 7.68 (td, J = 7.5, 1.3 Hz, 1H), 7.51 (s, 1H), 7.35 – 7.20 (m, 10H), 6.00 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 183.9, 181.8, 153.4, 143.8, 141.1, 135.2, 133.0, 132.8, 128.4, 128.2, 127.5, 127.2, 126.5, 126.4, 126.1, 124.9, 45.9; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{16}O_3Na$ 363.0997; Found 363.1003.

2-Hydroxy-3-tritylnaphthalene-1,4-dione (3g): orange oil (274 mg, 66% yield, hexane/EtOAc = 8/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 7.5 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.89 (s, 1H), 7.77 – 7.63 (m, 2H), 7.46 (d, J = 8.6 Hz, 6H), 7.21 (t, J = 7.7 Hz, 6H), 7.11 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.7, 145.6, 135.4, 134.3, 132.8, 129.4, 128.6, 127.5, 127.4, 125.9, 125.5, 61.3; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{20}O_3Na$ 439.1310; Found 439.1314.

2-Hydroxy-3-(1-(*p*-tolyl)ethyl)naphthalene-1,4-dione (3h): orange oil (207 mg, 71% yield, hexane/EtOAc = 8/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (ddd, J = 27.1, 7.7, 1.1 Hz, 2H), 7.67 (dtd, J = 33.9, 7.5, 1.3 Hz, 2H), 7.53 (d, J = 2.3 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 4.65 (q, J = 7.4 Hz, 1H), 2.29 (s, 3H), 1.71 (d, J = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 184.3, 182.0, 135.8, 135.1, 133.0, 129.2, 128.9, 127.7, 127.1, 127.1, 126.0, 21.1, 17.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{16}O_3Na$ 315.0997; Found 315.1002.

2-Hydroxy-3-(4-methoxybenzyl)naphthalene-1,4-dione (3i): orange oil (205 mg, 70% yield, hexane/EtOAc = 7/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, J = 20.5, 7.6 Hz, 2H),

7.74 (td, *J* = 7.6, 1.3 Hz, 1H), 7.67 (td, *J* = 7.5, 1.2 Hz, 1H), 7.41 (s, 1H), 7.32 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 2H), 3.75 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 184.5, 181.7, 158.1, 152.8, 135.0, 133.0, 131.0, 130.2, 129.39, 126.9, 126.1, 123.4, 113.9, 55.2, 28.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{14}O_4Na$ 317.0790; Found 317.0795. Physical and spectral properties of this material were identical to those previously reported in literature.[13]

3-(Ferrocenylmethyl)-2-hydroxy-1,4-naphthoquinone (3j): pale green powder (186 mg, 82% yield, hexane/EtOAc = 7/1 as the eluent). mp = 159–160 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.7 Hz, 1H), 8.03 (d, *J* = 6.8 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.36 (s, 1H), 4.26 (s, 2H), 4.16 (s, 5H), 4.03 (s, 2H), 3.65 (s, 2H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 184.3, 181.9, 152.5, 134.9, 132.9, 132.8, 129.4, 126.8, 126.1, 123.2, 85.7, 69.1, 68.8, 67.4, 23.2; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{16}FeO_3Na$ 395.0449; Found 395.0442. Physical and spectral properties of this material were identical to those previously reported in literature.[8b]

2-(10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulen-5-yl)-3-hydroxynaphthalene-1,4-dione (3k): orange solid (120 mg, 75% yield, hexane/EtOAc = 8/1 as the eluent). mp = 139–140 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.03 (m, 1H), 8.03 – 7.97 (m, 1H), 7.69 (td, *J* = 7.6, 1.2 Hz, 1H), 7.61 (td, *J* = 7.5, 1.1 Hz, 1H), 7.55 (s, 1H), 7.41 – 7.35 (m, 2H), 7.10 (dq, *J* = 5.0, 3.1, 1.9 Hz, 6H), 5.93 (s, 1H), 3.51 (m, 2H), 3.03 – 2.86 (m, 2H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 184.2, 182.1, 152.5, 141.4, 138.4, 135.2, 133.0, 132.9, 131.4, 129.9, 129.0, 127.3, 126.9, 126.3, 126.1, 125.8, 77.4, 77.1, 76.8, 48.9, 33.8; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{18}O_3Na$ 389.1154; Found 389.1148.

(*E*)-3-(1,3-Diphenylallyl)-4-hydroxy-2*H*-chromen-2-one (5a): white solid (329 mg, 93% yield,

hexane/EtOAc = 8/1 as the eluent). mp = 157–158 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.82 (m, 1H), 7.59 (t, *J* = 7.7 Hz, 1H), 7.45 (dt, *J* = 9.5, 4.6 Hz, 6H), 7.41 – 7.26 (m, 7H), 6.82 (dd, *J* = 16.1, 6.3 Hz, 1H), 6.58 (d, *J* = 16.1 Hz, 1H), 5.53 (d, *J* = 6.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3, 160.9, 152.8, 139.6, 136.2, 134.0, 132.2, 129.4, 128.7, 128.2, 128.1, 127.8, 126.6, 124.1, 123.2, 116.6, 115.9, 106.4, 44.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{18}O_3Na$ 377.1154; Found 377.1162. Physical and spectral properties of this material were identical to those previously reported in literature.[6]

(*E*)-3-(1,3-Di-*m*-tolylallyl)-4-hydroxy-2*H*-chromen-2-one (5b): white solid (294 mg, 77% yield, hexane/EtOAc = 8/1 as the eluent). mp = 177–179 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.7 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.41 – 7.30 (m, 4H), 7.26 (d, *J* = 5.0 Hz, 5H), 7.19 (d, *J* = 7.4 Hz, 1H), 7.13 (s, 1H), 6.94 (s, 1H), 6.75 (dd, *J* = 16.1, 6.2 Hz, 1H), 6.59 – 6.50 (m, 1H), 5.48 (d, *J* = 6.0 Hz, 1H), 2.39 (d, *J* = 7.3 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2, 160.8, 152.8, 139.53, 139.3, 138.3, 136.1, 133.9, 132.2, 129.3, 128.9, 128.6, 128.6, 127.3, 125.0, 123.7, 123.1, 116.5, 106.5, 43.9, 21.6, 21.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{22}O_3Na$ 405.1467; Found 405.1472.

(*E*)-3-(1,3-Di-*p*-tolylallyl)-4-hydroxy-2*H*-chromen-2-one (5c): white solid; (263 mg, 69% yield, hexane/EtOAc = 8/1 as the eluent). mp = 104–105 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.58 – 7.47 (m, 1H), 7.33 – 7.25 (m, 6H), 7.19 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 6.97 (s, 1H), 6.66 (dd, *J* = 16.1, 6.1 Hz, 1H), 6.49 (d, *J* = 16.1 Hz, 1H), 5.41 (d, *J* = 6.0 Hz, 1H), 2.34 (d, *J* = 8.0 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1, 160.8, 152.8, 138.0, 137.6, 136.4, 133.7, 133.4, 132.1, 130.1, 129.4, 128.0, 127.1, 126.5, 123.9, 123.1, 116.5, 116.0, 106.6, 43.7, 21.2, 21.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{22}O_3Na$ 405.1467;

Found 405.1469. Physical and spectral properties of this material were identical to those previously reported in literature.[11c]

(*E*)-3-(1,3-Bis(4-chlorophenyl)allyl)-4-hydroxy-2*H*-chromen-2-one (5d): white solid (350 mg, 83% yield, hexane/EtOAc = 8/1 as the eluent). mp = 170–172 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.8 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 7.42 – 7.30 (m, 11H), 7.05 (s, 1H), 6.77 (dd, J = 16.1, 6.2 Hz, 1H), 6.55 – 6.43 (m, 1H), 5.45 (d, J = 5.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.8, 159.8, 151.5, 136.6, 133.1, 132.8, 132.4, 131.9, 131.3, 128.3, 128.2, 127.7, 127.5, 126.6, 123.0, 122.0, 115.4, 114.5, 104.7, 42.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{16}Cl_2O_3Na$ 445.0374; Found 445.0376.

(*E*)-3-(1,3-Bis(4-bromophenyl)allyl)-4-hydroxy-2*H*-chromen-2-one (5e): white solid (443 mg, 87% yield, hexane/EtOAc = 7/1 as the eluent). mp = 159–161 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, J = 7.9, 1.2 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.47 (dd, J = 22.4, 8.4 Hz, 4H), 7.35 – 7.20 (m, 7H), 6.74 (dd, J = 16.1, 6.2 Hz, 1H), 6.44 (d, J = 16.1 Hz, 1H), 5.37 (d, J = 6.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.0, 161.0, 152.7, 138.3, 134.8, 133.2, 132.5, 132.4, 131.9, 129.8, 128.8, 128.1, 124.19, 123.1, 122.2, 121.7, 116.7, 115.7, 105.8, 43.7; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{16}Br_2O_3Na$ 534.9343; Found 534.9346.

3-Benzhydryl-4-hydroxy-2*H*-chromen-2-one (5f): white solid (251 mg, 80% yield, hexane/EtOAc = 8/1 as the eluent). mp = 176–178 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 7.38 (t, J = 7.2 Hz, 4H), 7.33 (dd, J = 7.6, 4.9 Hz, 3H), 7.26 (dd, J = 12.4, 7.4 Hz, 5H), 6.27 (s, 1H), 5.98 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2, 160.7, 152.8, 140.0, 132.2, 128.8, 127.9, 124.0, 123.2, 116.5, 116.0, 107.8, 47.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{16}O_3Na$ 351.0997; Found 351.0989. Physical and spectral properties of

this material were identical to those previously reported in literature.[14b]

3-(Bis(4-fluorophenyl)methyl)-4-hydroxy-2*H*-chromen-2-one (5g): white solid (317 mg, 87% yield, hexane/EtOAc = 8/1 as the eluent). mp = 175–177 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 7.9, 1.6 Hz, 1H), 7.57 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.39 – 7.34 (m, 4H), 7.33 – 7.24 (m, 3H), 7.24 – 7.15 (m, 4H), 5.91 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.4, 163.1 (d, J = 1.6 Hz), 161.0, 160.7 (d, J = 1.7 Hz), 152.7, 135.5 (d, J = 2.4 Hz), 132.4, 130.4, 130.3, 124.1, 123.2, 116.6, 116.3 (d, J = 0.6 Hz), 115.7, 107.5, 45.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.94; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{14}F_2O_3Na$ 387.0809; Found 387.0814. Physical and spectral properties of this material were identical to those previously reported in literature.[14b]

3-(Bis(4-chlorophenyl)methyl)-4-hydroxy-2*H*-chromen-2-one (5h): white solid (348 mg, 88% yield, hexane/EtOAc = 8/1 as the eluent). mp = 181–182 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, J = 8.0, 1.4 Hz, 1H), 7.62 – 7.50 (m, 1H), 7.37 – 7.01 (m, 10H), 5.92 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.1, 160.8, 152.7, 138.1, 133.9, 132.5, 130.1, 129.7, 124.2, 123.2, 116.6, 115.7, 107.0, 46.1.; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{22}H_{14}Cl_2O_3Na$ 419.0218; Found 419.0210. Physical and spectral properties of this material were identical to those previously reported in literature.[14b]

4-Hydroxy-3-trityl-2*H*-chromen-2-one (5i): white solid (287 mg, 71% yield, hexane/EtOAc = 8/1 as the eluent). mp = 186–188 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 6.8 Hz, 1H), 7.53 – 7.44 (m, 7H), 7.32 – 7.26 (m, 7H), 7.21 (q, J = 7.4 Hz, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.9, 152.7, 143.8, 132.0, 129.6, 128.3, 126.8, 123.6, 116.3, 116.1, 110.5, 60.9; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{28}H_{20}O_3Na$ 427.1310; Found 427.1316. Physical and spectral properties of this material were identical to those previously reported in literature.[14a]

4-Hydroxy-3-(1-(*p*-tolyl)ethyl)-2*H*-chromen-2-one (5j): white solid (193 mg, 69% yield, hexane/EtOAc = 8/1 as the eluent). mp = 168–170 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 1.5 Hz, 1H), 7.50 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.38 (d, J = 7.9 Hz, 2H), 7.30 (d, J = 8.3 Hz, 1H), 7.23 (q, J = 8.0 Hz, 3H), 4.69 (q, J = 7.2 Hz, 1H), 2.36 (s, 3H), 1.65 (d, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.6, 159.8, 152.5, 138.3, 137.7, 131.8, 130.5, 127.2, 123.8, 122.9, 116.4, 116.2, 110.1, 34.2, 21.1, 16.6; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{16}O_3Na$ 303.0997; Found 303.0991. Physical and spectral properties of this material were identical to those previously reported in literature.[14b]

4-Hydroxy-3-(4-methoxybenzyl)-2*H*-chromen-2-one (5k): white solid (220 mg, 78% yield, hexane/EtOAc = 8/1 as the eluent). mp = 187–189 ℃. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.79 (dd, J = 8.2, 1.5 Hz, 1H), 7.45 – 7.39 (m, 1H), 7.21 – 7.15 (m, 2H), 6.98 (d, J = 8.7 Hz, 2H), 6.63 (d, J = 8.7 Hz, 2H), 3.63 (s, 2H), 2.39 – 2.24 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 163.3, 160.7, 158.0, 152.4, 132.3, 132.1, 129.6, 124.4, 123.8, 116.7, 116.7, 114.1, 105.2, 55.5, 28.7; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{14}O_4Na$ 305.0790; Found 305.0795. Physical and spectral properties of this material were identical to those previously reported in literature.[14b]

4-Hydroxy-3-(1-(*p*-tolyl)but-3-en-1-yl)-2*H*-chromen-2-one (5l): white solid (175 mg, 57% yield, hexane/EtOAc = 8/1 as the eluent). mp = 179–181 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (t, J = 5.7 Hz, 1H), 7.41 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.30 (d, J = 8.0 Hz, 2H), 7.22 – 7.05 (m, 4H), 5.80 (ddt, J = 17.0, 10.2, 6.8 Hz, 1H), 5.09 – 4.82 (m, 2H), 4.60 (t, J = 7.7 Hz, 1H), 2.84 (qt, J = 14.3, 7.2 Hz, 2H), 2.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.5, 160.0, 152.6, 137.7, 137.2, 135.8, 131.8, 130.4, 127.7, 123.8, 122.8, 117.3, 116.4, 116.0, 108.6, 39.5, 35.2, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.17; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}O_3Na$ 329.1154;

Found 329.1151.

(*E*)-3-(1,3-Diphenylallyl)-4-hydroxy-6-methyl-2*H*-chromen-2-one (5m): white solid (316 mg, 86% yield, hexane/EtOAc = 8/1 as the eluent). mp = 191–192 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.44 – 7.18 (m, 13H), 6.76 (dd, J = 16.1, 6.3 Hz, 1H), 6.51 (d, J = 14.9 Hz, 1H), 5.47 (d, J = 6.1 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.5, 161.0, 150.9, 139.9, 136.3, 133.8, 133.2, 129.3, 128.7, 128.4, 128.4, 128.1, 128.0, 127.6, 126.6, 122.8, 116.3, 115.6, 106.4, 44.0, 21.3; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{20}O_3Na$ 391.1310; Found 391.1316. Physical and spectral properties of this material were identical to those previously reported in literature.[6]

(*E*)-3-(1,3-Diphenylallyl)-6-fluoro-4-hydroxy-2*H*-chromen-2-one (5n): white solid (275 mg, 74% yield, hexane/EtOAc = 8/1 as the eluent). mp = 188–190 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, J = 8.4, 2.8 Hz, 1H), 7.42 – 7.22 (m, 12H), 6.73 (dd, J = 16.1, 6.3 Hz, 1H), 6.52 (d, J = 16.1 Hz, 1H), 5.45 (d, J = 5.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.8, 160.0 (d, J = 3.1 Hz), 157.4, 148.8 (d, J = 1.6 Hz), 139.2, 136.0, 134.2, 129.4, 128.7, 128.2, 128.0, 127.9, 127.7, 126.6, 119.6 (d, J = 24.8 Hz), 118.1 (d, J = 8.3 Hz), 116.8 (d, J = 9.1 Hz), 108.9 (d, J = 25.4 Hz), 107.2, 44.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{17}FO_3Na$ 395.1059; Found 395.1067.

(*E*)-6-Bromo-3-(1,3-diphenylallyl)-4-hydroxy-2*H*-chromen-2-one (5o): white solid (337 mg, 78% yield, hexane/EtOAc = 8/1 as the eluent). mp = 187–189 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 2.3 Hz, 1H), 7.62 (dd, J = 8.8, 2.4 Hz, 1H), 7.43 – 7.15 (m, 13H), 6.73 (dd, J = 16.1, 6.3 Hz, 1H), 6.52 (dd, J = 16.1, 1.4 Hz, 1H), 5.44 (dd, J = 6.3, 1.7 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6, 159.7, 151.5, 139.2, 136.0, 135.0, 134.2, 129.5, 128.7, 128.2, 128.1, 127.9, 127.7, 126.6, 125.9, 118.3, 117.5, 116.8, 107.3, 44.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for

$C_{24}H_{17}BrO_3Na$ 455.0259; Found 455.0253.

(*E*)-3-(1,3-Diphenylallyl)-4-hydroxyquinolin-2(1*H*)-one (5p): white solid (141 mg, 40% yield, hexane/EtOAc = 7/1 as the eluent). mp = 189–191 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.48 – 7.11 (m, 15H), 6.86 – 6.79 (m, 1H), 6.53 (d, J = 16.1 Hz, 1H), 5.79 (d, J = 5.9 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.8, 159.3, 140.6, 137.6, 136.5, 133.3, 130.9, 129.2, 129.2, 128.6, 128.3, 127.9, 127.3, 126.6, 122.8, 122.1, 115.8, 115.5, 111.7, 43.0; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{19}NO_2Na$ 376.1313; Found 376.1317.

(*E*)-4-Amino-3-(1,3-diphenylallyl)-2*H*-chromen-2-one (5q): white solid (318 mg, 90% yield, hexane/EtOAc = 5/1 as the eluent). mp = 156–158 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 1H), 7.46 – 7.34 (m, 5H), 7.33 – 7.17 (m, 8H), 6.73 (dd, J = 15.9, 7.0 Hz, 1H), 6.56 (d, J = 16.0 Hz, 1H), 5.57 (d, J = 6.9 Hz, 1H), 5.06 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3, 152.8, 149.7, 140.8, 137.0, 132.6, 131.7, 128.9, 128.6, 127.7, 127.6, 127.2, 127.0, 126.4, 123.6, 120.8, 117.5, 114.8, 100.4, 44.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{19}NO_2Na$ 376.1313; Found 376.1315.

4-Hydroxy-3-(1-phenylpropyl)-2*H*-chromen-2-one (5r): white solid (757 mg, 54% yield, hexane/EtOAc = 8/1 as the eluent). mp = 179–182 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 8.0, 1.3 Hz, 1H), 7.48 – 7.37 (m, 3H), 7.33 (t, J = 7.6 Hz, 2H), 7.27 – 7.12 (m, 3H), 6.45 (s, 1H), 4.46 (t, J = 7.7 Hz, 1H), 2.26 – 1.94 (m, 2H), 0.99 (t, J = 7.3 Hz, 3H).; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.8, 160.0, 152.6, 141.2, 131.8, 129.6, 127.7, 127.6, 123.8, 122.8, 116.4, 116.0, 108.9, 41.7, 24.0, 12.4.; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{16}O_3Na$ 303.0997; Found 303.1002. Physical and spectral properties of this material were identical to those previously reported in literature.[15]

4-Hydroxy-3-(1,2,3,4-tetrahydronaphthalen-1-yl)-2*H*-chromen-2-one (5s): white solid (950 mg, 65% yield, hexane/EtOAc = 8/1 as the eluent). mp = 173–175 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.52 (ddd, *J* = 8.8, 7.4, 1.6 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.26 (s, 1H), 7.25 (s, 2H), 7.24 – 7.17 (m, 2H), 5.86 (s, 1H), 4.62 (t, *J* = 6.9 Hz, 1H), 2.92 (t, *J* = 5.0 Hz, 2H), 2.28 – 2.18 (m, 1H), 1.99 – 1.82 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.7, 159.9, 152.5, 138.1, 134.6, 131.8, 130.6, 129.6, 128.0 127.5, 123.9, 123.0 116.4, 116.2, 109.4, 36.4, 29.8, 29.3, 21.7; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{16}O_3Na$ 315.0997; Found 315.0992. Physical and spectral properties of this material were identical to those previously reported in literature.[14b]

(*E*)-3-(1-(Benzo[*d*][1,3]dioxol-5-yl)-4,4-dimethylpent-2-en-1-yl)-4-hydroxy-2*H*-chromen-2-one (5t): white solid (1.47 g, 78% yield, hexane/EtOAc = 8/1 as the eluent). mp = 156–157 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.9, 1.4 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.34 – 7.26 (m, 3H), 6.78 (s, 3H), 5.96 (s, 2H), 5.91 (dd, J = 16.0, 5.5 Hz, 1H), 5.65 (dd, J = 16.0, 1.8 Hz, 1H), 5.13 (dd, J = 5.4, 1.6 Hz, 1H), 1.05 (s, 9H).; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.0, 161.0, 152.7, 148.4, 147.0, 146.8, 133.5, 132.1, 124.4, 123.9, 123.1, 120.9, 116.5, 116.0, 108.8, 108.6, 106.4, 101.2, 43.5, 33.4, 29.4.; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{22}O_5Na$ 401.1365; Found 401.1363.

General Procedure for Preparation of 6 and 7

A mixture of the substrate **1a** or **4a** (1.2 mmol), substrate **2** (1.0 mmol), in HFIP (5.0 mL) was stirred at room temperature for 10 min. Extra DDQ (1.0 equiv) was added to the reaction mixture after the alkylation reaction of **1a** or **4a** with **2** was completed. The mixture was continued to be stirred for 1h at room temperature. Upon completion of the reaction, the resulted mixture was

concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) to give the pure product **6** and **7**.

2,4-Diphenyl-2*H*-benzo[*g*]chromene-5,10-dione (6a): orange oil (284 mg, 78% yield, hexane/EtOAc = 7/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 7.6 Hz, 1H), 7.75 (t, J = 8.3 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.58 (s, 1H), 7.42 (d, J = 7.6 Hz, 4H), 7.30 (t, J = 7.6 Hz, 4H), 7.21 (t, J = 6.7 Hz, 2H), 7.01 (dd, J = 15.8, 9.0 Hz, 1H), 6.62 (d, J = 15.8 Hz, 1H), 5.39 (d, J = 9.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.3, 179.4, 154.8, 138.6, 137.5, 135.2, 134.3, 133.2, 132.2, 131.1, 129.4, 128.9, 128.1, 127.8, 127.7, 127.4, 126.7, 126.1, 124.2, 121.0, 78.1; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{16}O_3Na$ 387.0997; Found 387.1000. Physical and spectral properties of this material were identical to those previously reported in literature.[6]

2,4-Bis(4-chlorophenyl)-2*H*-benzo[*g*]chromene-5,10-dione (6b): orange oil (307 mg, 71% yield, hexane/EtOAc = 7/1 as the eluent). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 1H), 8.01 – 7.95 (m, 1H), 7.76 – 7.65 (m, 2H), 7.48 (d, J = 8.5 Hz, 2H), 7.36 (dd, J = 11.0, 8.5 Hz, 4H), 7.19 (d, J = 8.4 Hz, 2H), 6.11 (d, J = 4.6 Hz, 1H), 5.91 (d, J = 4.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 181.2, 179.2, 136.8, 135.8, 135.5, 134.5, 133.9, 133.5, 132.0, 130.9, 129.2, 129.0, 128.7, 128.4, 126.7, 126.2, 123.8, 120.6; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{14}Cl_2O_3Na$ 455.0218; Found 455.0221.

2,4-Diphenyl-2*H*,5*H*-pyrano[3,2-*c*]chromen-5-one (7a): white solid (282 mg, 80% yield, hexane/EtOAc = 7/1 as the eluent). mp = 158–160 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.2 Hz, 1H), 7.60 (t, J = 6.2 Hz, 3H), 7.46 (d, J = 7.4 Hz, 3H), 7.42 – 7.39 (m, 5H), 7.33 (d, J = 4.7 Hz, 1H), 7.30 (s, 2H), 6.19 (d, J = 4.1 Hz, 1H), 5.81 (d, J = 4.1 Hz, 1H); ^{13}C{^{1}H} NMR (100

MHz, $CDCl_3$) δ 161.4, 153.6, 137.9, 135.3, 132.6, 129.3, 128.9, 128.0, 127.5, 127.5, 124.0, 123.3, 120.3, 1167, 115.3, 102.9; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{16}O_3Na$ 375.0997; Found 375.1001. Physical and spectral properties of this material were identical to those previously reported in literature.[6]

2,4-Di-*m*-tolyl-2*H*,5*H*-pyrano[3,2-*c*]chromen-5-one (7b): white solid (186 mg, 49% yield, hexane/EtOAc = 7/1 as the eluent). mp = 157-159 ℃. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 7.9, 1.5 Hz, 1H), 7.53 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.35 (d, J = 2.6 Hz, 2H), 7.30 (dt, J = 8.0, 3.9 Hz, 2H), 7.26 (s, 1H), 7.21 (d, J = 8.1 Hz, 1H), 7.18 – 7.11 (m, 4H), 6.08 (d, J = 4.1 Hz, 1H), 5.73 (d, J = 4.1 Hz, 1H), 2.37 (d, J = 4.3 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4, 158.7, 153.6, 138.7, 138.3, 137.9, 137.5, 135.2, 132.5, 130.0, 128.8, 128.7, 128.2, 128.1, 127.8, 124.7, 124.5, 123.9, 123.3, 120.3, 116.6, 115.3, 102.9, 79.0, 21.5, 21.5; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{20}O_3Na$ 403.1310; Found 403.1316.

2,4-Di-*p*-tolyl-2*H*,5*H*-pyrano[3,2-*c*]chromen-5-one (7c): light yellow oil (213 mg, 56% yield, hexane/EtOAc = 7/1 as the eluent). ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 9.1 Hz, 1H), 7.52 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.29 (d, J = 8.3 Hz, 1H), 7.22 (t, Hz, 5H), 7.17 (d, J = 8.0 Hz, 2H), 6.09 (d, J = 4.2 Hz, 1H), 5.73 (d, J = 4.3 Hz, 1H), 2.37 (d, J = 5.6 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.3, 153.6, 139.3, 137.6, 135.2, 135.0, 132.5, 129.6, 128.7, 127.7, 127.3, 123.9, 123.3, 119.8, 116.6, 115.4, 102.9, 21.3, 21.3; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{20}O_3Na$ 403.1310; Found 403.1313.

2,4-Bis(4-bromophenyl)-2*H*,5*H*-pyrano[3,2-*c*]chromen-5-one (7d): light yellow oil (376 mg, 74% yield, hexane/EtOAc = 7/1 as the eluent). ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, J = 8.9 Hz, 1H), 7.55 (d, J = 8.3 Hz, 3H), 7.48 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 7.35 – 7.27 (m, 2H),

7.19 (d, *J* = 8.4 Hz, 2H), 6.09 (d, *J* = 4.3 Hz, 1H), 5.71 (d, *J* = 4.3 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4, 153.6, 136.9, 136.6, 134.7, 133.0, 132.2, 131.1, 129.2, 129.1, 124.2, 123.6, 123.3, 122.1, 116.8, 114.9, 102.4; HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{14}Br_2O_3Na$ 532.9187; Found 532.9193.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:

NMR (^{1}H, ^{13}C) spectra (PDF)

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Notes

The authors declare no competing financial interest.

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