JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Tunable Synthesis of 3-Acyl-2-naphthols and 3-Substituted Isocoumarins via Jones Reagent Promoted Cascade Reactions of 2-(4-Hydroxy-but-1-ynyl)benzaldehydes

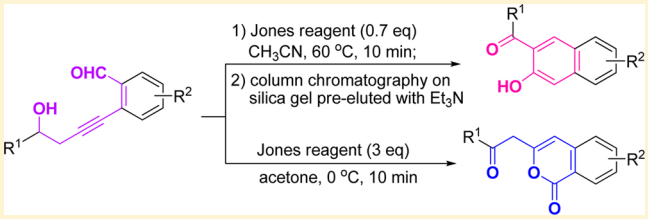
Yan He,[†,‡] Xinying Zhang,[‡] Nana Shen,[‡] and Xuesen Fan*[,†,‡]

[†]School of Environment, Key Laboratory for Yellow River and Huai River Water Environment and Pollution Control, Ministry of Education, Henan Normal University, Xinxiang, Henan 453007, PR China

[‡]School of Chemistry and Chemical Engineering, Key Laboratory of Green Chemical Media and Reactions, Ministry of Education, Henan Normal University, Xinxiang, Henan 453007, PR China

Supporting Information

ABSTRACT: Novel and efficient synthesis of 3-acyl-2-naphthols and 3-substituted isocoumarins via the tunable cascade reactions of 2-(4-hydroxy-but-1-ynyl)benzaldehydes have been developed. Treatment of 2-(4-hydroxy-but-1-ynyl)benzaldehydes with 0.7 equiv of Jones reagent in CH_3CN and subsequent purification through column chromatography on silica gel pre-eluted with Et_3N afforded 3-acyl-2-naphthols with high efficiency. When the same substrates were treated with 3 equiv of Jones reagents in acetone, on the other hand, 3-substituted isocoumarins could be obtained in good yields.



INTRODUCTION

During our recent study on functionalized allenes, we have been trying to prepare a 1,2-allenic ketone derivative, 2-(4-oxo-4-phenylbuta-1,2-dienyl)benzaldehyde (**A**), based on an envisioned synthetic pathway as shown in Scheme 1.

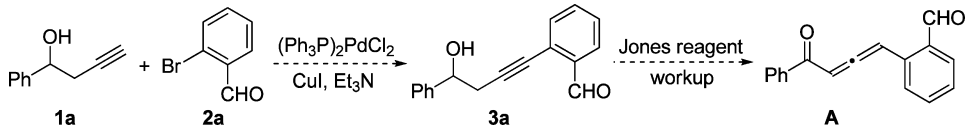
The synthetic work started with the coupling reaction of 1-phenylbut-3-yn-1-ol (**1a**) with 2-bromobenzaldehyde (**2a**) under standard conditions,[1] which afforded 2-(4-hydroxy-4-phenylbut-1-ynyl)benzaldehyde (**3a**) in 90% yield (Scheme 2). Following oxidation of **3a** with Jones reagent, however, did not give the expected allenic ketone **A**.[2] Instead, 2-(4-oxo-4-phenylbut-1-ynyl)benzaldehyde (**4a**) was formed together with 3-benzoyl-2-naphthol (**5a**) and 3-(2-oxo-2-phenylethyl)-1*H*-isochromen-1-one (**6a**). Moreover, it was observed that **4a** could be cleanly converted into 3-benzoyl-2-naphthol (**5a**) upon purification via column chromatography on silica gel pre-eluted with Et_3N (Scheme 2).

Although the envisioned 1,2-allenic ketone was not obtained from the reaction of **3a**, we realized that the unexpected formation of **5a** and **6a** might be more rewarding. First, (*o*-hydroxyaryl)(aryl)methanones are the basic scaffolds of a plethora of compounds with remarkable biological activities.[3] In particular, 3-acyl-2-naphthols like **5a** and their derivatives have been used as building blocks of compounds with valuable applications in chemical, medicinal as well as material fields.[4−6] Notwithstanding their importance, efficient synthetic methods toward 3-acyl-2-naphthols are surprisingly limited. While Friedel−Crafts acylation of phenols or Fries-type rearrangement of suitable aryl esters are the most frequently used methods to prepare (*o*-hydroxyaryl)(aryl)methanone derivatives, these strategies are not applicable for the synthesis of 3-acyl-2-naphthols, mainly because of selectivity and/or reactivity problems. For example, Hashimoto et al. observed that efficient benzoylation of 2-naphthol needed 10 equiv of benzoyl chloride in neat TfOH, and the reaction mainly gave 1-benzoyl-2-naphthol rather than 3-benzoyl-2-naphthol (Scheme 3).[7] It was also found that the Fries rearrangement of 2-naphthyl benzoate, another likely route leading to 3-benzoyl-2-naphthol, did not take place at all under the catalysis of TfOH.[7] Park et al. observed that the reaction of 2-methoxynaphthalene with benzoyl chloride in the presence of $AlCl_3$ gave 1-benzoyl-2-naphthol in 77% yield, but no 3-benzoyl-2-naphthol was obtained.[8] To solve these problems, Kozlowski et al. developed a pathway toward 3-aroyl-2-naphthol in which 2-methoxynaphthalene was first *ortho*-lithiated and then treated with a Weinreb amide to give 3-benzoyl-2-methoxynaphthalene. Subsequent demethylation of 3-benzoyl-2-methoxynaphthalene with BCl_3 afforded the desired 3-benzoyl-2-naphthol (Scheme 3).[5] While this elegant strategy is reliable, the usage of powerful base and naphthalene precursors may dent its application scope and substrate generality. On the other hand, it is well-known that isocoumarins are ubiquitous structural units in a plethora of natural products with remarkable biological interests and the majority of the naturally occurring isocoumarins that are of polyketide origin possess a C-3 substituent.[9−11] As a result, developing practical and convenient synthetic protocols for isocoumarins has always been a hot topic in the synthetic community.[12] On the basis of the above facts, the

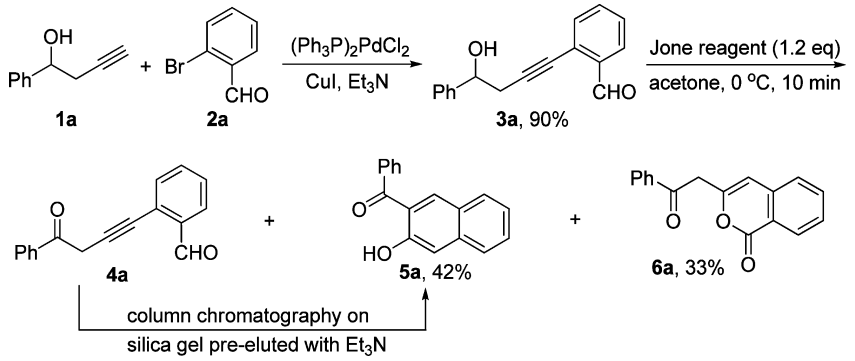
Received: July 22, 2013
Published: September 12, 2013

   dx.doi.org/10.1021/jo401502k | *J. Org. Chem.* 2013, 78, 10178−10191

Scheme 1. Envisioned Synthetic Pathway toward 1,2-Allenic Ketone A



Scheme 2. Unexpected Formation of 5a and 6a from the Reaction of 3a



Scheme 3. Literature Synthetic Pathways toward 3-Benzoyl-2-naphthol (5a)

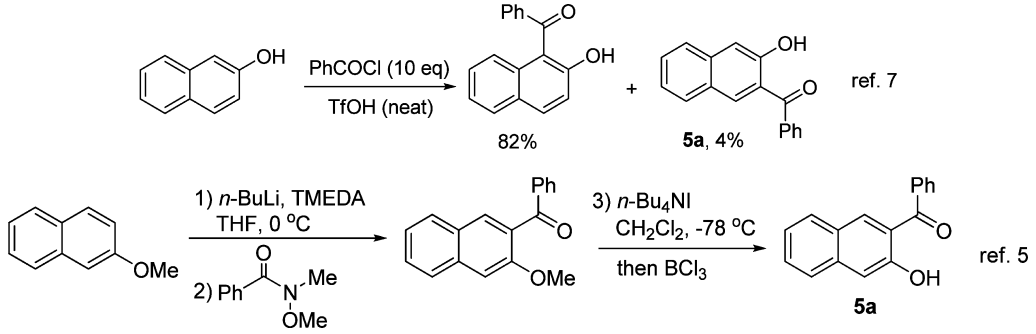
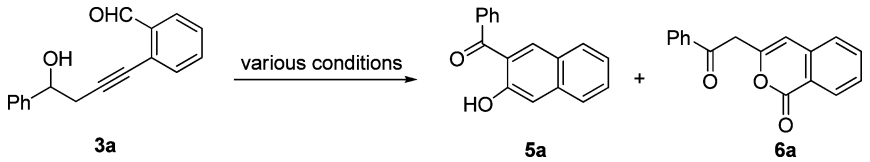


Table 1. Optimization Study for the Synthesis of 5a and 6a from 3a[a]



					yield (%)[b]	
entry	amount of oxidant (equiv)	solvent	T (°C)	t (min)	**5a**	**6a**
1	1.2	acetone	0	10	42	33
2	1.8	acetone	0	10	21	43
3	2.4	acetone	0	10	10	50
4	**3**	**acetone**	**0**	**10**	**trace**	**68**
5	3	acetone	−10	10	trace	69
6	3	acetone	reflux	10	31	42
7	0.7	acetone	0	20	50	15
8	0.7	acetone	reflux	10	62	9
9	**0.7**	**CH_3CN**	**60**	**10**	**75**	**trace**
10	0.7	CH_2Cl_2	reflux	30	35	8
11	0.7	THF	60	30	48	7

[a]Reaction conditions: **3a** (0.5 mmol), solvent (5 mL). [b]Isolated yield after column chromatography on silica gel pre-eluted with Et_3N.

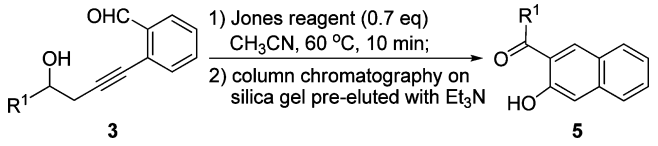
formation of **5a** and **6a** from readily obtainable **3a** under mild conditions validates its potentiality as alternative protocols for the synthesis of 3-acyl-2-naphthols and 3-substituted isocoumarins and deserves further exploration.

RESULTS AND DISCUSSION

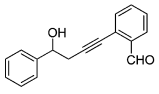
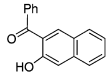
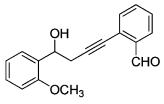
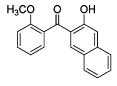
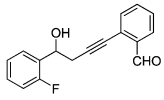
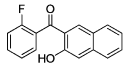
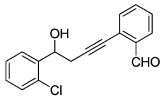
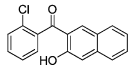
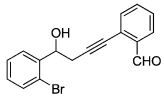
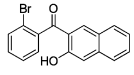
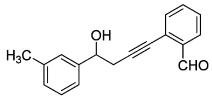
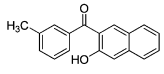
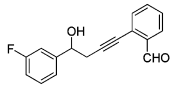
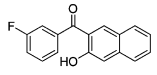
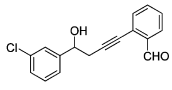
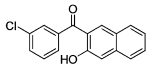
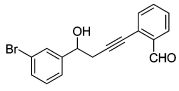
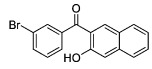
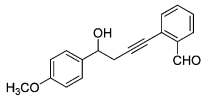
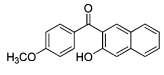
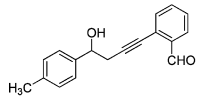
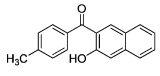
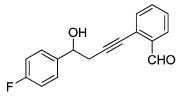
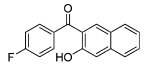
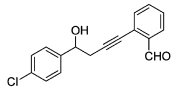
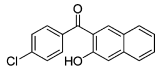
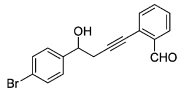
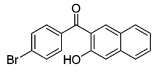
On the basis of the above facts, optimization studies to make the reaction of **3a** proceed in a more selective manner to give either **5a** or **6a** as the main product were carried out. Thus, **3a** was

dx.doi.org/10.1021/jo401502k | J. Org. Chem. 2013, 78, 10178−10191

Table 2. Synthesis of 3-Acyl-2-naphthols 5a–5w[a]

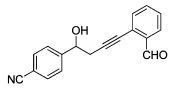
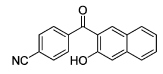
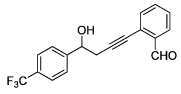
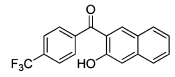
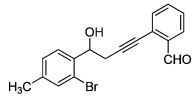
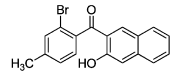
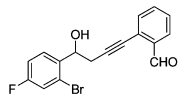
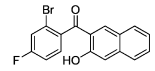
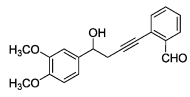
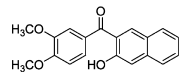
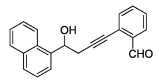
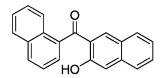
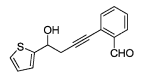
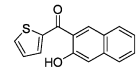
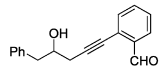
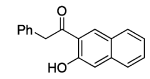
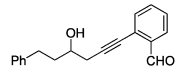
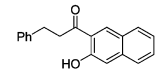


3 5

Entry	Substrates (3)	Products (5)	Yield (%)[b]
1	 3a	 5a	75
2	 3b	 5b	72
3	 3c	 5c	68
4	 3d	 5d	75
5	 3e	 5e	73
6	 3f	 5f	65
7	 3g	 5g	68
8	 3h	 5h	71
9	 3i	 5i	73
10	 3j	 5j	76
11	 3k	 5k	74
12	 3l	 5l	66[c]
13	 3m	 5m	67
14	 3n	 5n	76

dx.doi.org/10.1021/jo401502k | J. Org. Chem. 2013, 78, 10178–10191

Table 2. continued

Entry	Substrates (**3**)	Products (**5**)	Yield (%)[b]
15	 **3o**	 **5o**	74
16	 **3p**	 **5p**	73
17	 **3q**	 **5q**	67
18	 **3r**	 **5r**	72
19	 **3s**	 **5s**	71
20	 **3t**	 **5t**	66
21	 **3u**	 **5u**	65
22	 **3v**	 **5v**	67
23	 **3w**	 **5w**	72

[a]**3** (1 mmol), Jones reagent (0.7 mmol), CH_3CN (10 mL), 60 °C, 10 min. [b]Isolated yield. [c]Confirmed by X-ray diffraction analysis.

treated with varied amounts of oxidant under different reaction temperatures (Table 1). First, we observed that with Jones reagent more than 1.2 equiv, the yield of **6a** increased while that of **5a** decreased accordingly (entries 2−4). When **3a** was treated with 3 equiv of Jones reagent in acetone at 0 °C for 10 min, **6a** could be obtained in 68% yield (entry 4). With the same amount of oxidant, lower temperature (−10 °C) resulted in similar yield of **6a** as that of 0 °C (entry 5). On the other hand, higher temperature (in refluxing acetone) gave decreased yield of **6a** but increased yield of **5a** (entry 6). Next, the reaction of **3a** was tried with Jones reagent in an amount less than 1.2 equiv. We found that after **3a** was treated with 0.7 equiv of Jones reagent in acetone at 0 °C for 20 min, **5a** and **6a** were obtained in yields of 50 and 15%, respectively (entry 7). Further optimization showed that higher temperature facilitated the transformation of **3a** toward **5a** (entry 8). Finally, different solvents were also tried as possible media (entries 9−11). It turned out that **5a** could be obtained in a yield of 75% by treating **3a** with Jones reagent in CH_3CN at 60 °C for 10 min (entry 9). Under similar conditions, using CH_2Cl_2 and THF as the solvent gave lower yields of **5a** (entries 10 and 11).

With the optimized conditions in hand, we first screened a range of 2-(4-hydroxy-but-1-ynyl)benzaldehydes (**3**) to probe the scope of the new synthetic strategy toward 3-acyl-2-naphthols **5** (Table 2). It turns out that the R^1 unit of **3** can be either electron-rich (Table 2, entries 2, 6, 10, 11 and 19) or electron-deficient (entries 3−5, 7−9, 12−16 and 18) phenyl, naphthyl (entry 20), thienyl (entry 21) or alkyl groups (entries 22 and 23) to afford the corresponding 3-acyl-2-naphthols **5b**−**5w** with yields ranging from 65 to 76% without showing obvious electronic and steric effects.

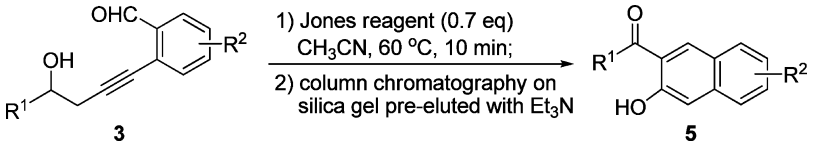
Moreover, it was demonstrated that the aldehyde moiety of **3** with R^2 as methyl or fluoro group is also suitable for the 3-acyl-naphthols synthesis to give **5x**−**5cc** in yields ranging from 65 to 74% (Table 3). These results suggest that the newly developed 3-acyl-2-naphthols synthesis will find a broad range of applications.

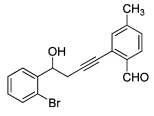
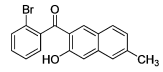
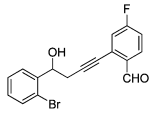
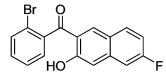
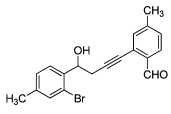
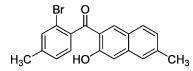
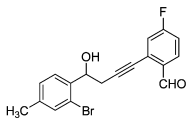
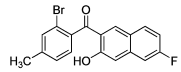
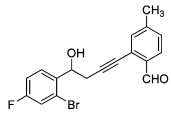
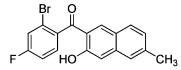
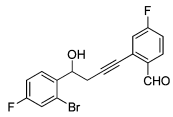
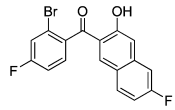
In the next stage, the generality and scope for the synthesis of 3-substituted isocoumarins (**6**) from the tandem reaction of **3** was studied. As shown in Table 4, the reaction is compatible with an array of 2-(4-hydroxy-but-1-ynyl)benzaldehydes bearing either electron-withdrawing or electron-donating substituents attached on the *ortho*, *meta*, or *para* positions (entries 1−18), and all the substrates participated in this tandem reaction efficiently to give the corresponding 3-substituted isocoumarins **6a**−**6r** in reasonably good yields.

On the basis of the above observations, plausible pathways to account for the formation of **5a** and **6a** from **3a** were proposed as shown in Scheme 4. Initially, oxidation of **3a** by Jones reagent gives 3-yn-1-one **4a**. In the presence of an excess amount of Jones reagent, **4a** is further oxidized to give 2-(4-oxo-4-phenylbut-1-ynyl)benzoic acid (**I**). Under the reaction conditions, the carboxyl group in **I** is protonated to initiate an *intramolecular* Michael-type (6-*endo*) cyclization to give isocoumarin **6a**.[13] On the other hand, in the presence of only 0.7 equiv of Jones reagent,

dx.doi.org/10.1021/jo401502k | J. Org. Chem. 2013, 78, 10178−10191

Table 3. Synthesis of 3-Acyl-2-naphthols 5x−5cc[a]



Entry	Substrates (**3**)	Products (**5**)	Yield (%)[b]
1	 **3x**	 **5x**	68
2	 **3y**	 **5y**	66
3	 **3z**	 **5z**	74
4	 **3aa**	 **5aa**	73
5	 **3bb**	 **5bb**	67
6	 **3cc**	 **5cc**	65

[a]Reaction conditions: **3** (1 mmol), Jones reagent (0.7 mmol), CH_3CN (10 mL), 60 °C, 10 min. [b]Isolated yield.

the oxidation mainly gives **4a**. Isomerization of **4a** affords its allenic ketone counterpart (**A**),[14] which then undergoes a nucleophilic hydration to give an enol intermediate (**II**). Following *intramolecular* Knoevenagel condensation of **II** results in a cyclic enone (**III**). Aromatization of **III** affords **5a** as the final product.

Recently, Wang et al. revealed that 1,3-dihydroxy-12*H*-benzo[*b*]xanthen-12-one (**7**, Scheme 5) was capable of inhibiting yeast's α-glucosidase 17-fold more strongly than its xanthone counterpart that has smaller conjugated π-system.[15] Moreover, Na et al. found the bisepoxyl derivative of **7** showed significant cancer cell growth inhibition against the HT29 and DU145 cell lines.[16] We noticed that in the aforementioned two studies, compound **7** was prepared through the condensation of 3-hydroxy-2-naphthoic acid with phloroglucinol in the presence of anhydrous zinc chloride in refluxing phosphoryl chloride.[15,16] To circumvent the usage of naphthalene precursor and harsh and strictly anhydrous conditions employed in the above-mentioned processes, we tried to prepare **7** with an alternative procedure based on the synthetic strategy developed herein. Thus, 2-(4-(2-bromo-4,6-dimethoxyphenyl)-4-hydroxybut-1-ynyl)benzaldehyde (**3hh**) was treated with Jones reagent to give (2-bromo-4,6-dimethoxyphenyl)(3-hydroxynaphthalen-2-yl)methanone (**5dd**), which was then transformed into **5ee** upon treatment with BBr_3. Subsequent base-promoted *intramolecular O*-arylation of **5ee** afforded **7** with high efficiency (Scheme 5).

CONCLUSION

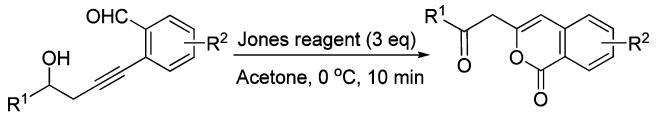
In summary, we have developed a tunable synthesis of 3-acyl-2-naphthols and 3-substituted isocoumarins via Jones reagent promoted cascade reactions of the readily obtainable 2-(4-hydroxy-but-1-ynyl)benzaldehydes. Treatment of 2-(4-hydroxy-but-1-ynyl)benzaldehydes with 0.7 equiv of Jones reagent initiated a tandem process including oxidation, isomerization, hydration, *intramolecular* Knovengel condensation and aromatization to afford 3-acyl-2-naphthols in good yields. By using this strategy, an alternative synthetic pathway toward the pharmaceutically attractive 1,3-dihydroxy-12*H*-benzo[*b*]xanthen-12-one was developed. On the other hand, when 2-(4-hydroxy-but-1-ynyl)benzaldehydes were treated with excess amount of Jones reagent, another version of cascade process took place, and the biologically and synthetically interesting 3-substituted isocoumarin could be obtained with good efficiency. Compared with literature procedures toward 3-acyl-2-naphthols and 3-substituted isocoumarin, the strategies developed herein showed advantages such as readily available starting materials and more practical reaction conditions.

EXPERIMENTAL SECTION

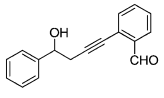
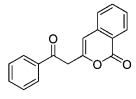
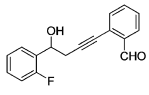
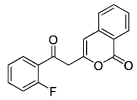
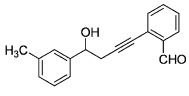
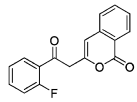
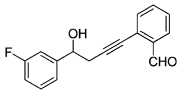
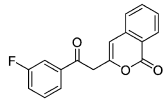
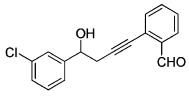
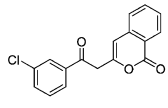
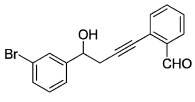
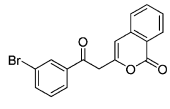
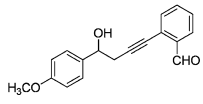
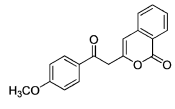
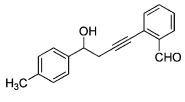
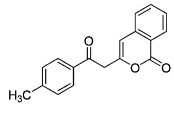
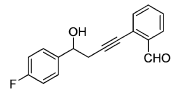
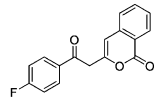
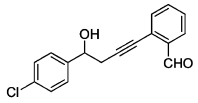
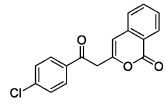
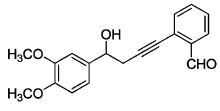
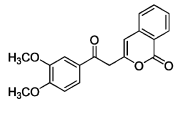
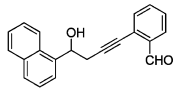
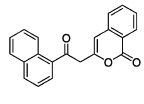
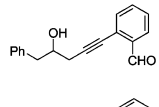
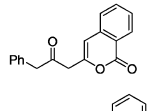
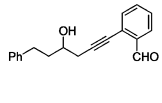
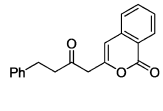
General Methods. 2-(4-Hydroxy-but-1-ynyl)benzaldehydes (**3**) were prepared through coupling of but-3-yn-1-ols (**1**) with 2-bromobenzaldehydes (**2**) based on literature method.[1] Melting points were recorded with a micromelting point apparatus and uncorrected. ^1H

dx.doi.org/10.1021/jo401502k | J. Org. Chem. 2013, 78, 10178−10191

Table 4. Synthesis of 3-Substituted Isocoumarins 6a−6r[a]

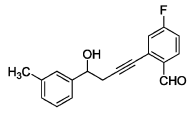
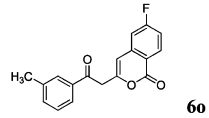
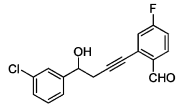
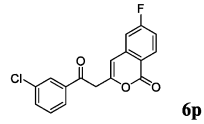
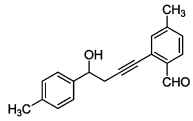
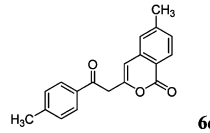
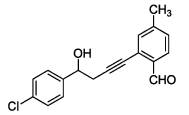
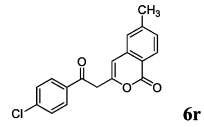


3 6

Entry	Substrates (3)	Products (6)	Yield (%)[b]
1	 3a	 6a	68
2	 3c	 6b	52
3	 3f	 6c	66
4	 3g	 6d	58
5	 3h	 6e	60
6	 3i	 6f	62
7	 3j	 6g	70
8	 3k	 6h	67
9	 3l	 6i	60
10	 3m	 6j	61
11	 3s	 6k	75
12	 3t	 6l	73
13	 3v	 6m	62
14	 3w	 6n	60

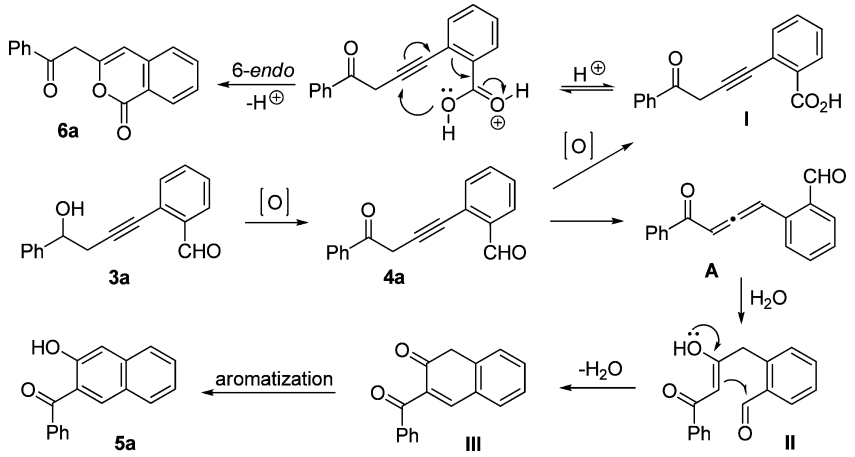
dx.doi.org/10.1021/jo401502k | J. Org. Chem. 2013, 78, 10178−10191

Table 4. continued

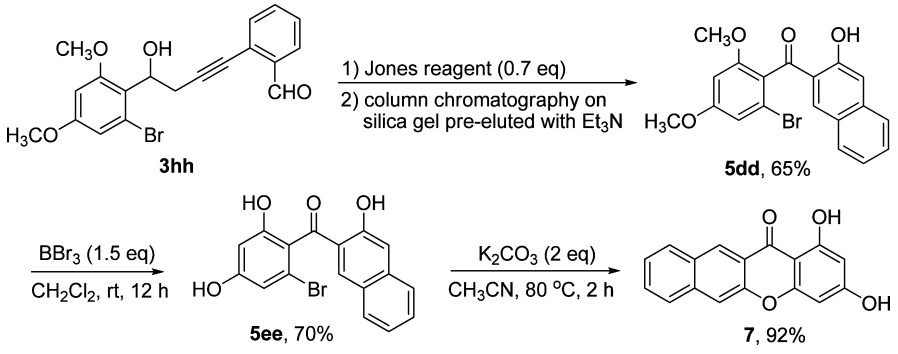
Entry	Substrates (**3**)	Products (**6**)	Yield (%)[b]
15	 **3dd**	 **6o**	67
16	 **3ee**	 **6p**	58
17	 **3ff**	 **6q**	66
18	 **3gg**	 **6r**	60

[a]Reaction conditions: **3** (1 mmol), Jones reagent (3 mmol), acetone (10 mL), 0 °C, 10 min. [b]Isolated yield.

Scheme 4. Plausible Mechanism for the Formation of 5a and 6a from 3a



Scheme 5. Alternative Synthetic Pathway toward Compound 7



and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts were reported in ppm from tetramethylsilane (TMS) as internal standard in $CDCl_3$ solutions. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets); td (triplet of doublets); br s (broad singlet), etc. Coupling constants are given in Hz. High-resolution mass spectra (HRMS) were obtained by using a MicroTOF mass spectrometer. All reactions were monitored by thin-layer chromatography (TLC) using silica gel plates (silica gel 60 F_{254} 0.25 mm).

Typical Procedure for the Synthesis of 3a and Spectroscopic Data of 3a–3hh. To a flask containing 1-phenylbut-3-yn-1-ol (**1a**, 2 mmol) and 2-bromobenzaldehyde (**2a**, 2.4 mmol) in Et_3N (8 mL) were added $Pd(PPh_3)_2Cl_2$ (0.04 mmol) and CuI (0.02 mmol). After the mixture was stirred at 50 °C under N_2 atmosphere for 2 h, the reaction was quenched with aqueous NH_4Cl and extracted with ethyl acetate (10

dx.doi.org/10.1021/jo401502k | J. Org. Chem. 2013, 78, 10178–10191

mL × 3). The combined organic layers were washed with water and brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated under a vacuum, and the crude product was purified by chromatography on silica gel by using petroleum ether−ethyl acetate (5:1) as the eluent to afford **3a**. **3b**−**3hh** were prepared in a similar manner.

2-(4-Hydroxy-4-phenylbut-1-ynyl)benzaldehyde (3a). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (450 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89−2.94 (m, 2H), 3.50 (s, 1H), 4.97 (t, J = 6.4 Hz, 1H), 7.26−7.50 (m, 8H), 7.80 (d, J = 8.0 Hz, 1H), 10.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 72.5, 79.0, 94.0, 125.9, 126.6, 128.0, 128.2, 128.5, 133.4, 133.8, 136.0, 142.8, 192.3; MS m/z 251 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{15}O_2$ 251.1072 [M + H], found 251.1066.

2-(4-Hydroxy-4-(2-methoxyphenyl)but-1-ynyl)benzaldehyde (3b). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (515 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92−3.09 (m, 2H), 3.26 (s, 1H), 3.87 (s, 3H), 5.20 (t, J = 5.6 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H), 7.26−7.50 (m, 6H), 7.84 (d, J = 7.6 Hz, 1H), 10.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.6, 55.3, 69.2, 78.6, 94.5, 110.4, 120.8, 127.0, 127.7, 128.1, 128.9, 130.3, 133.4, 133.7, 136.0, 156.2, 192.3; MS m/z 281 [MH]; HRMS (ESI) calcd for $C_{18}H_{17}O_3$ 281.1177 [M + H], found 281.1182.

2-(4-(2-Fluorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3c). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (477 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92−3.07 (m, 2H), 5.32−5.35 (m, 1H), 7.04−7.62 (m, 7H), 7.85 (d, J = 6.8 Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.5, 66.61, 66.63, 79.5, 93.1, 115.2, 115.5, 124.37, 124.41, 126.1, 127.2, 127.3, 128.3, 128.8, 129.4, 129.5, 129.7, 133.5, 133.7, 136.1, 158.4, 160.9, 192.1; MS m/z 269 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}FO_2$ 269.0978 [M + H], found 269.0980.

2-(4-(2-Chlorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3d). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (511 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84−3.10 (m, 3H), 5.41 (t, J = 5.0 Hz, 1H), 7.22−7.52 (m, 6H), 7.68 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.2 Hz, 1H), 10.28 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 68.8, 79.4, 93.3, 126.1, 127.12, 127.15, 128.3, 128.8, 129.0, 129.4, 131.6, 133.5, 133.8, 136.0, 139.9, 192.2; MS m/z 285 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}ClO_2$ 285.0682 [M + H], found 285.0677.

2-(4-(2-Bromophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3e). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (577 mg, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.83−3.11 (m, 3H), 5.36 (t, J = 5.6 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.34−7.54 (m, 5H), 7.68 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 10.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 71.0, 79.4, 93.3, 121.7, 126.1, 127.4, 127.7, 128.3, 128.8, 129.3, 132.6, 133.5, 133.8, 136.0, 141.4, 192.2; MS m/z 329 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}BrO_2$ 329.0177 [M + H], found 329.0179.

2-(4-Hydroxy-4-*m*-tolylbut-1-ynyl)benzaldehyde (3f). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (480 mg, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.94 (d, J = 6.8 Hz, 3H), 4.97 (d, J = 2.4 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 7.22−7.51 (m, 6H), 7.84 (d, J = 8.0 Hz, 1H), 10.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 30.6, 72.6, 79.0, 93.9, 122.9, 126.50, 126.53, 128.2, 128.3, 128.5, 128.9, 133.4, 133.7, 136.1, 138.3, 142.6, 192.1; MS m/z 265 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{17}O_2$ 265.1229 [M + H], found 265.1226.

2-(4-(3-Fluorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3g). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (466 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92−2.94 (m, 2H), 5.02 (t, J = 6.0 Hz, 1H), 6.99−7.54 (m, 7H), 7.85 (d, J = 7.2 Hz, 1H), 10.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 71.8, 79.7, 93.1, 112.7, 112.9, 114.8, 115.0, 121.40, 121.43, 125.9, 128.4, 129.0, 130.06, 130.14, 133.5, 133.8, 136.1, 145.2, 145.3, 161.7, 164.2, 192.0; MS m/z 269 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}FO_2$ 269.0978 [M + H], found 269.0989.

2-(4-(3-Chlorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3h). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (494 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (d, J = 6.8 Hz, 2H), 3.71−3.72 (m, 1H), 4.96 (t, J = 6.6 Hz, 1H), 7.21−7.53 (m, 7H), 7.82 (d, J = 8.0 Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 71.7, 79.5, 93.3, 124.0, 126.10, 126.15, 128.1, 128.4, 128.6, 129.8, 133.5, 133.8, 134.4, 136.0, 144.9, 192.0; MS m/z 285 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}ClO_2$ 285.0682 [M + H], found 285.0681.

2-(4-(3-Bromophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3i). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (590 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (d, J = 6.8 Hz, 2H), 3.46 (s, 1H), 4.95 (t, J = 6.2 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.33−7.51 (m, 5H), 7.60 (s, 1H), 7.82 (d, J = 7.6 Hz, 1H), 10.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 71.7, 79.6, 93.2, 122.6, 124.5, 126.0, 128.4, 128.7, 129.0, 130.1, 131.0, 133.5, 133.8, 136.0, 145.0, 192.1; MS m/z 329 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}BrO_2$ 329.0177 [M + H], found 329.0178.

2-(4-Hydroxy-4-(4-methoxyphenyl)but-1-ynyl)benzaldehyde (3j). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (515 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (t, J = 6.4 Hz, 2H), 3.32 (s, 1H), 3.77 (s, 3H), 4.91 (d, J = 5.2 Hz, 1H), 6.87 (d, J = 9.2 Hz, 2H), 7.31−7.47 (m, 5H), 7.80 (d, J = 7.6 Hz, 1H), 10.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 55.3, 72.2, 78.8, 94.1, 113.9, 126.7, 127.1, 127.9, 128.2, 133.4, 133.7, 135.0, 136.0, 159.3, 192.2; MS m/z 281 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{17}O_3$ 281.1178 [M + H], found 281.1175.

2-(4-Hydroxy-4-*p*-tolylbut-1-ynyl)benzaldehyde (3k). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (475 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.91−2.93 (m, 2H), 3.05 (s, 1H), 4.95 (d, J = 5.6 Hz, 1H), 7.17 (d, J = 6.4 Hz, 2H), 7.30−7.49 (m, 5H), 7.82 (d, J = 7.6 Hz, 1H), 10.24−10.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 30.5, 72.4, 78.9, 94.0, 125.7, 126.6, 128.0, 128.2, 129.2, 133.4, 133.6, 136.1, 137.8, 139.7, 192.1; MS m/z 265 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{17}O_2$ 265.1229 [M + H], found 265.1233.

2-(4-(4-Fluorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3l). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (482 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.79−2.90 (m, 2H), 4.26 (s, 1H), 4.90 (t, J = 6.6 Hz, 1H), 6.95 (t, J = 8.8 Hz, 2H), 7.24−7.40 (m, 5H), 7.70 (d, J = 7.6 Hz, 1H), 10.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.5, 71.7, 78.9, 94.0, 115.1, 115.3, 126.6, 127.6, 127.7, 127.9, 128.2, 133.4, 133.8, 135.9, 138.79, 138.82, 161.1, 163.5, 192.3; MS m/z 269 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}FO_2$ 269.0978 [M + H], found 269.0982.

2-(4-(4-Chlorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3m). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (506 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 (d, J = 6.4 Hz, 2H), 4.96 (t, J = 6.2 Hz, 1H), 7.27−7.51 (m, 7H), 7.81 (d, J = 8.0 Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 71.8, 79.5, 93.3, 126.0, 127.2, 128.4, 128.6, 128.8, 133.5, 133.7, 133.8, 136.0, 141.2, 192.1; MS m/z 285 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}ClO_2$ 285.0682 [M + H], found 285.0677.

2-(4-(4-Bromophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3n). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (597 mg, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 (d, J = 6.0 Hz, 2H), 3.39 (s, 1H), 4.94 (t, J = 5.6 Hz, 1H), 7.30 (d, J = 8.4 Hz, 2H), 7.41−7.52 (m, 5H), 7.82−7.84 (m, 1H), 10.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 71.8, 79.5, 93.2, 121.8, 126.0, 127.6, 128.4, 128.9, 131.6, 133.5, 133.8, 136.0, 141.7, 192.1; MS m/z 329 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{14}BrO_2$ 329.0177 [M + H], found 329.0182.

4-(4-(2-Formylphenyl)-1-hydroxybut-3-ynyl)benzonitrile (3o). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (468 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90−2.94 (m, 2H), 5.07 (t, J = 6.0 Hz, 1H), 7.46 (d, J = 8.0 Hz, 2H), 7.52−7.57 (m, 3H), 7.65 (d, J = 8.0 Hz, 2H), 7.83 (d, J = 8.0 Hz, 1H), 10.24 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 71.6, 111.6, 118.8, 126.6, 128.6, 132.3, 132.4, 133.5, 133.9, 136.0, 147.9, 192.0; MS m/z 276 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{14}NO_2$ 276.1025 [M + H], found 276.1026.

2-(4-Hydroxy-4-(4-(trifluoromethyl)phenyl)but-1-ynyl)-benzaldehyde (3p). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (547 mg, 86%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91−2.94 (m, 3H), 5.07 (t, J = 5.8 Hz, 1H), 7.41−7.63 (m, 7H), 7.83 (d, J = 7.6 Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.8, 71.8, 79.9, 92.8, 125.4, 125.45, 125.52, 126.1, 128.4, 129.4, 133.5, 133.8, 135.9, 146.5, 192.0; MS m/z 319 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{13}F_3NaO_2$ 341.0765 [M + Na], found 341.0762.

2-(4-(2-Bromo-4-methylphenyl)-4-hydroxybut-1-ynyl)-benzaldehyde (3q). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (595 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (t, J = 2.8 Hz, 3H), 2.84−3.08 (m, 2H), 3.27 (s, 1H), 5.29−5.32 (m, 1H), 7.15 (d, J = 5.6 Hz, 1H), 7.35−7.56 (m, 5H), 7.83 (d, J = 5.6 Hz, 1H), 10.29 (t, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 29.0, 71.0, 79.3, 93.5, 121.5, 126.3, 127.1, 128.3, 128.6, 133.1, 133.5, 133.8, 136.1, 138.4, 139.5, 192.2; MS m/z 343 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{16}BrO_2$ 343.0334 [M + H], found 343.0334.

2-(4-(2-Bromo-4-fluorophenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3r). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (588 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78−3.07 (m, 2H), 3.56 (s, 1H), 5.31 (s, 1H), 7.04−7.09 (m, 1H), 7.25−7.28 (m, 1H), 7.40−7.52 (m, 3H), 7.64−7.68 (m, 1H), 7.83 (d, J = 6.4 Hz, 1H), 10.30 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.1, 70.6, 79.7, 93.1, 114.8, 115.0, 119.7, 119.9, 121.5, 121.6, 125.8, 128.4, 128.5, 128.6, 129.2, 133.5, 133.8, 136.0, 137.5, 160.5, 163.0, 192.2; MS m/z 347 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{13}BrFO_2$ 347.0083 [M + H], found 347.0088.

2-(4-(3,4-Dimethoxyphenyl)-4-hydroxybut-1-ynyl)benzaldehyde (3s). Eluent, petroleum ether−ethyl acetate (3:1). Yellow liquid (577 mg, 93%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.72−2.83 (m, 2H), 3.66 (s, 3H), 3.67 (s, 3H), 3.98 (s, 1H), 4.78 (t, J = 6.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.78 (d, J = 8.4 Hz, 1H), 6.86 (s, 1H), 7.18 (t, J = 7.0 Hz, 1H), 7.26−7.32 (m, 2H), 7.62 (d, J = 8.0 Hz, 1H), 10.11 (s, 1H). ^{13}NMR (100 MHz, $CDCl_3$) δ 30.5, 55.7, 55.8, 72.1, 78.6, 94.4, 108.9, 110.9, 118.1, 126.7, 127.6, 128.0, 133.2, 133.7, 135.7, 135.9, 148.4, 148.8, 192.2; MS m/z 311 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{19}O_4$ 311.1283 [M + H], found 311.1286.

2-(4-Hydroxy-4-(naphthalen-2-yl)but-1-ynyl)benzaldehyde (3t). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (552 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.04−3.22 (m, 2H), 5.79−5.82 (m, 1H), 7.40−7.57 (m, 6H), 7.78−7.92 (m, 4H), 8.12 (d, J = 8.4 Hz, 1H), 10.31 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9, 69.4, 79.6, 93.8, 122.8, 123.1, 125.5, 125.7, 126.3, 128.3, 128.58, 128.62, 129.1, 130.2, 133.5, 133.7, 133.8, 136.1, 138.0, 192.0; MS m/z 301 $[MH]^+$; HRMS (ESI) calcd for $C_{21}H_{17}O_2$ 301.1129 [M + H], found 301.1130.

2-(4-Hydroxy-4-(thiophen-2-yl)but-1-ynyl)benzaldehyde (3u). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (461 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00 (d, J = 6.4 Hz, 2H), 3.85 (s, 1H), 5.21 (t, J = 6.4 Hz, 1H), 6.93−6.96 (m, 1H), 7.04 (d, J = 2.4 Hz, 1H), 7.22−7.24 (m, 1H), 7.32−7.35 (m, 1H), 7.45 (t, J = 2.4 Hz, 2H), 7.77−7.79 (m, 1H), 10.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 68.6, 79.4, 93.4, 124.2, 125.0, 126.6, 126.7, 128.0, 128.3, 133.4, 133.8, 136.0, 146.6, 192.3; MS m/z 257 $[MH]^+$; HRMS (ESI) calcd for $C_{15}H_{13}O_2S$ 257.0636 [M + H], found 257.0629.

2-(4-Hydroxy-5-phenylpent-1-ynyl)benzaldehyde (3v). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (486 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.61−2.74 (m, 2H), 2.89−3.00 (m, 3H), 4.12 (t, J = 6.2 Hz, 1H), 7.21−7.54 (m, 8H), 7.85 (d, J = 7.6 Hz, 1H), 10.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.6, 42.9, 71.1, 79.2, 94.2, 126.67, 126.70, 128.28, 128.30, 128.7, 129.5, 133.6, 133.8, 136.1, 137.9, 192.1; MS m/z 265 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{17}O_2$ 265.1229 [M + H], found 265.1228.

2-(4-Hydroxy-6-phenylhex-1-ynyl)benzaldehyde (3w). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (500 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.95−2.00 (m, 2H), 2.70−2.91 (m, 4H), 3.49 (s, 1H), 3.94 (t, J = 5.8 Hz, 1H), 7.18−7.38 (m, 6H), 7.47−7.50 (m, 2H), 7.84 (d, J = 7.2 Hz, 1H), 10.44 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.7, 32.0, 38.2, 69.4, 79.0, 94.4, 126.0, 126.7, 128.3, 128.4, 128.5, 133.6, 133.9, 136.0, 141.8, 192.2; MS m/z 279 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{19}O_2$ 279.1385 [M + H], found 279.1380.

2-(4-(2-Bromophenyl)-4-hydroxybut-1-ynyl)-4-methylbenzaldehyde (3x). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (616 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.81−3.10 (m, 2H), 5.33−5.37 (m, 1H), 7.16−7.36 (m, 4H), 7.51−7.54 (m, 1H), 7.67−7.74 (m, 2H), 10.22 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 29.0, 71.1, 79.7, 92.8, 121.7, 126.0, 127.5, 127.8, 129.2, 129.3, 132.7, 133.9, 134.0, 141.5, 144.9, 191.9; MS m/z 343 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{16}BrO_2$ 343.0334 [M + H], found 343.0335.

2-(4-(2-Bromophenyl)-4-hydroxybut-1-ynyl)-4-fluorobenzaldehyde (3y). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (630 mg, 91%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85−3.10 (m, 2H), 3.26 (s, 1H), 5.37 (d, J = 3.2 Hz, 1H), 7.07−7.19 (m, 3H), 7.34−7.38 (m, 1H), 7.52−7.87 (m, 3H), 10.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 71.0, 78.2, 94.9, 116.1, 116.3, 120.0, 120.3, 121.7, 127.4, 127.8, 128.9, 129.5, 131.2, 131.3, 132.7, 132.78, 132.81, 141.4, 164.3, 166.9, 190.6; MS m/z 347 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{13}BrFO_2$ 347.0083 [M + H], found 347.0085.

2-(4-(2-Bromo-4-methylphenyl)-4-hydroxybut-1-ynyl)-4-methylbenzaldehyde (3z). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (655 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.37 (s, 3H), 2.81−3.18 (m, 3H), 5.31 (t, J = 3.6 Hz, 1H), 7.14−7.21 (m, 2H), 7.30 (s, 1H), 7.35 (s, 1H), 7.52−7.54 (m, 1H), 7.72−7.75 (m, 1H), 10.22 (t, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 21.6, 29.0, 71.0, 79.5, 92.9, 121.5, 126.1, 127.1, 128.6, 128.9, 129.3, 133.1, 133.9, 134.0, 138.4, 139.5, 144.8, 191.9; MS m/z 357 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{18}BrO_2$ 357.0490 [M + H], found 357.0488.

2-(4-(2-Bromo-4-methylphenyl)-4-hydroxybut-1-ynyl)-4-fluorobenzaldehyde (3aa). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (634 mg, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (d, J = 1.6 Hz, 3H), 2.85−3.07 (m, 3H), 5.31−5.33 (m, 1H), 7.07−7.16 (m, 3H), 7.35 (s, 1H), 7.51−7.54 (m, 1H), 7.83−7.86 (m, 1H), 10.21 (t, J = 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 28.9, 70.8, 78.0, 95.0, 116.0, 116.3, 120.0, 120.2, 121.5, 127.1, 128.6, 129.1, 131.0, 131.1, 132.8, 133.1, 138.3, 139.7, 164.3, 166.9, 190.6; MS m/z 361 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{15}BrFO_2$ 361.0239 [M + H], found 361.0233.

2-(4-(2-Bromo-4-fluorophenyl)-4-hydroxybut-1-ynyl)-4-methylbenzaldehyde (3bb). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (612 mg, 85%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.78−3.06 (m, 2H), 3.70 (br s, 1H), 5.28−5.31 (m, 1H), 7.05−7.08 (m, 1H), 7.20−7.29 (m, 3H), 7.64−7.72 (m, 2H), 10.22 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 29.1, 70.6, 79.9, 92.5, 114.8, 115.0, 119.6, 119.8, 121.46, 121.54, 125.7, 128.56, 128.64, 129.4, 129.5, 133.8, 134.0, 137.6, 144.9, 160.5, 162.9, 191.9; MS m/z 361 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{15}BrFO_2$ 361.0239 [M + H], found 361.0246.

2-(4-(2-Bromo-4-fluorophenyl)-4-hydroxybut-1-ynyl)-4-fluorobenzaldehyde (3cc). Eluent, petroleum ether−ethyl acetate (5:1). Yellow liquid (612 mg, 84%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80−3.06 (m, 2H), 3.48 (s, 1H), 5.30 (d, J = 10.0 Hz, 1H), 7.08−7.28 (m, 4H), 7.65 (t, J = 7.2 Hz, 1H), 7.83−7.87 (m, 1H), 10.24 (t, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.0, 70.5, 78.4, 94.6, 114.9, 115.1, 116.1, 116.4, 119.7, 119.9, 120.1, 120.3, 121.5, 121.6, 128.5, 128.6, 128.7, 131.5, 131.6, 132.8, 137.4, 160.5, 163.0, 164.3, 190.6; MS m/z 365 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}BrF_2O_2$ 364.9989 [M + H], found 364.9990.

4-Fluoro-2-(4-hydroxy-4-*m*-tolylbut-1-ynyl)benzaldehyde (3dd). Eluent, petroleum ether−ethyl acetate (5:1). Yellow oil (508 mg, 90%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.89−2.91 (m, 2H), 3.75 (br s, 1H), 4.91 (t, J = 6.4 Hz, 1H), 6.98−7.10 (m, 3H), 7.18−7.25 (m, 3H), 7.76−7.80 (m, 1H), 10.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 30.4, 72.4, 95.8, 115.9, 116.1, 119.8, 120.0, 122.9, 126.6, 128.4, 128.8, 129.4, 129.5, 130.4, 130.5, 132.8, 138.2, 142.8, 164.3, 166.9, 190.6; MS m/z 283 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{16}FO_2$ 283.1134 [M + H], found 283.1141.

2-(4-(3-Chlorophenyl)-4-hydroxybut-1-ynyl)-4-fluorobenzaldehyde (3ee). Eluent, petroleum ether−ethyl acetate (5:1). Yellow oil (532 mg, 88%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88 (d, J = 6.0 Hz, 2H), 3.95 (br s, 1H), 4.92 (t, J = 6.0 Hz, 1H), 7.03−7.09 (m, 2H), 7.24 (s, 3H), 7.40 (s, 1H), 7.76−7.79 (m, 1H), 10.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.4, 71.7, 95.0, 116.1, 116.3, 119.9, 120.2, 124.0, 126.1, 128.1, 129.8, 130.8, 130.9, 132.7, 134.4, 144.8, 164.3, 166.9, 190.5; MS m/z 303 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{13}ClFO_2$ 303.0588 [M + H], found 303.0563.

2-(4-Hydroxy-4-*p*-tolylbut-1-ynyl)-4-methylbenzaldehyde (3ff). Eluent, petroleum ether−ethyl acetate (5:1). Yellow oil (512 mg, 92%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.34 (s, 3H), 2.89−

2.91 (m, 2H), 3.50 (br s, 1H), 4.93 (t, J = 6.4 Hz, 1H), 7.15−7.32 (m, 6H), 7.70 (d, J = 8.0 Hz, 1H), 10.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 21.5, 30.5, 72.4, 79.0, 93.7, 125.8, 126.7, 128.1, 129.1, 129.2, 133.8, 133.9, 137.6, 139.9, 144.7, 191.9; MS m/z 279 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{19}O_2$ 279.1385 [M + H], found 279.1386.

2-(4-(4-Chlorophenyl)-4-hydroxybut-1-ynyl)-4-methylbenzaldehyde (3gg). Eluent, petroleum ether−ethyl acetate (5:1). Yellow oil (530 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.86 (d, J = 6.4 Hz, 2H), 3.98 (s, 1H), 4.91 (t, J = 6.4 Hz, 1H), 7.12−7.33 (m, 6H), 7.65 (d, J = 7.6 Hz, 1H), 10.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 30.6, 71.7, 79.5, 93.1, 126.3, 127.3, 128.5, 128.6, 129.3, 133.5, 133.8, 133.9, 141.5, 144.9, 191.8; MS m/z 299 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{16}ClO_2$ 299.0839 [M + H], found 299.0848.

2-(4-(2-Bromo-4,6-dimethoxyphenyl)-4-hydroxybut-1-ynyl)-benzaldehyde (3hh). Eluent, petroleum ether−ethyl acetate (3:1). Yellow oil (675 mg, 87%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.08 (d, J = 7.6 Hz, 2H), 3.81 (s, 3H), 3.86 (s, 3H), 5.41−5.43 (m, 1H), 6.46 (d, J = 1.2 Hz, 1H), 6.72 (d, J = 1.6 Hz, 1H), 7.34−7.47 (m, 3H), 7.82 (d, J = 8.0 Hz, 1H), 10.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.9, 55.6, 55.8, 72.5, 77.8, 94.3, 99.3, 109.6, 121.7, 124.3, 126.7, 127.6, 128.0, 133.3, 133.6, 136.1, 158.9, 160.2, 192.3; MS m/z 389 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{18}BrO_4$ 389.0388 [M + H], found 389.0377.

Typical Procedure for the Synthesis of (3-Hydroxynaphthalen-2-yl)(phenyl)methanone (5a). To a solution of 2-(4-hydroxy-4-phenylbut-1-ynyl)benzaldehyde (**3a**, 1 mmol) in CH_3CN (10 mL) was added Jones reagent (0.7 mmol), and the resulting mixture was stirred at 60 °C for 10 min. The resulting mixture was quenched with isopropanol and filtered, and the filtrate was concentrated under a vacuum. The residue was purified by column chromatography on silica gel pre-eluted with Et_3N (0.2 mL) by using petroleum ether−ethyl acetate (10:1) as the eluent to give (3-hydroxynaphthalen-2-yl)(phenyl)methanone (**5a**). **5b**−**5dd** were obtained in a similar manner.

(3-Hydroxynaphthalen-2-yl)(phenyl)methanone (5a).[5] Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (186 mg, 75%): mp 153−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, J = 7.6 Hz, 1H), 7.39 (s, 1H), 7.52−7.58 (m, 3H), 7.65−7.79 (m, 5H), 8.17 (s, 1H), 11.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.4, 121.0, 124.1, 126.3, 126.7, 128.5, 129.61, 129.63, 129.9, 132.4, 136.7, 137.9, 138.0, 157.4, 201.8; MS m/z 249 $[MH]^+$.

(3-Hydroxynaphthalen-2-yl)(2-methoxyphenyl)methanone (5b). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (200 mg, 72%): mp 113−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (s, 3H), 7.05−7.12 (m, 2H), 7.24−7.28 (m, 1H), 7.35−7.38 (m, 2H), 7.48−7.69 (m, 4H), 7.99 (s, 1H), 11.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 111.6, 112.0, 120.6, 121.8, 123.9, 126.3, 126.9, 127.7, 129.2, 129.7, 129.9, 132.3, 137.2, 138.2, 156.8, 157.4, 202.5; MS m/z 279 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_3$ 279.1021 [M + H], found 279.1028.

(2-Fluorophenyl)(3-hydroxynaphthalen-2-yl)methanone (5c). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (181 mg, 68%): mp 161−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26−7.36 (m, 4H), 7.51−7.61 (m, 3H), 7.70 (d, J = 8.4 Hz, 2H), 8.03 (s, 1H), 11.20 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.3, 116.4, 116.6, 121.4, 124.2, 124.5, 126.3, 126.4, 126.9, 129.7, 130.2, 133.2, 133.3, 137.0, 138.3, 157.0, 160.6, 198.8; MS m/z 267 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}FO_2$ 267.0821 [M + H], found 267.0830.

(2-Clorophenyl)(3-hydroxynaphthalen-2-yl)methanone (5d). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (212 mg, 75%): mp 141−142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (t, J = 7.4 Hz, 1H), 7.37 (s, 1H), 7.42−7.54 (m, 5H), 7.63−7.69 (m, 2H), 7.89 (s, 1H), 11.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.5, 121.0, 124.2, 126.3, 126.88, 126.91, 128.9, 129.7, 130.3, 131.0, 131.6, 137.2, 137.4, 138.5, 157.2, 201.0; MS m/z 283 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}ClO_2$ 283.0526 [M + H], found 283.0522.

(2-Bromophenyl)(3-hydroxynaphthalen-2-yl)methanone (5e). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (238 mg, 73%): mp 119−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (t, J = 7.0 Hz, 1H), 7.37−7.53 (m, 5H), 7.64−7.72 (m, 3H), 7.86 (s, 1H), 11.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.5, 119.4, 120.7, 124.2, 126.4, 126.9, 127.4, 128.8, 129.8, 130.3, 131.6, 133.4, 137.3, 138.5, 139.4, 157.3, 201.6; MS m/z 327 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}BrO_2$ 327.0021 [M + H], found 327.0018.

(3-Hydroxynaphthalen-2-yl)(*m*-tolyl)methanone (5f). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (170 mg, 65%): mp 93−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 7.30−7.59 (m, 7H), 7.73 (t, J = 7.8 Hz, 2H), 8.18 (s, 1H), 11.18 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 112.3, 121.1, 124.1, 126.3, 126.7, 126.9, 128.3, 129.6, 129.8, 130.0, 133.1, 136.8, 137.9, 138.0, 138.6, 157.3, 202.1; MS m/z 263 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_2$ 263.1072 [M + H], found 263.1073.

(3-Fluorophenyl)(3-hydroxynaphthalen-2-yl)methanone (5g). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (181 mg, 68%): mp 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.37 (m, 3H), 7.46−7.53 (m, 4H), 7.69−7.74 (m, 2H), 8.14 (s, 1H), 11.00 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 116.3, 116.6, 119.3, 119.5, 120.6, 124.3, 125.4, 126.3, 126.7, 129.6, 130.1, 130.2, 130.3, 136.6, 138.0, 139.8, 157.1, 161.2, 163.7, 200.2; MS m/z 267 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}FO_2$ 267.0821 [M + H], found 267.0825.

(3-Chlorophenyl)(3-hydroxynaphthalen-2-yl)methanone (5h). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (200 mg, 71%): mp 90−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 7.6 Hz, 1H), 7.38 (s, 1H), 7.47−7.75 (m, 7H), 8.11 (s, 1H), 10.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 120.7, 124.3, 126.4, 126.7, 127.7, 129.4, 129.7, 129.8, 130.1, 132.3, 134.8, 136.6, 138.1, 139.5, 157.2, 200.2; MS m/z 283 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}ClO_2$ 283.0526 [M + H], found 283.0528.

(3-Bromophenyl)(3-hydroxynaphthalen-2-yl)methanone (5i). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (238 mg, 73%): mp 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.45 (m, 3H), 7.55 (t, J = 7.4 Hz, 1H), 7.66−7.78 (m, 4H), 7.90 (d, J = 1.6 Hz. 1H), 8.11 (s, 1H), 10.98 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 120.6, 122.8, 124.3, 126.4, 126.7, 128.1, 129.7, 130.07, 130.15, 132.3, 135.2, 136.6, 138.1, 139.7, 157.2, 200.1; MS m/z 327 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}BrO_2$ 327.0021 [M + H], found 327.0016.

(3-Hydroxynaphthalen-2-yl)(4-methoxyphenyl)methanone (5j).[5] Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (211 mg, 76%): mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.93 (s, 3H), 7.04 (d, J = 8.8 Hz, 2H), 7.32 (t, J = 7.6 Hz, 1H), 7.37 (s, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.70−7.82 (m, 4H), 8.18 (s, 1H), 11.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.6, 112.3, 113.8, 121.4, 124.0, 126.3, 126.7, 129.5, 129.6, 130.4, 132.3, 136.0, 137.6, 157.2, 163.3, 200.1; MS m/z 279 $[MH]^+$.

(3-Hydroxynaphthalen-2-yl)(*p*-tolyl)methanone (5k). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (194 mg, 74%): mp 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 (s, 3H), 7.30−7.38 (m, 4H), 7.51−7.55 (m, 1H), 7.69−7.74 (m, 4H), 8.19 (s, 1H), 11.15 (d, J = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 112.3, 121.2, 124.0, 126.3, 126.7, 129.2, 129.5, 129.6, 129.9, 135.2, 136.4, 137.8, 143.2, 157.3, 201.4; MS m/z 263 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_2$ 263.1072 [M + H], found 263.1078.

(4-Fluorophenyl)(3-hydroxynaphthalen-2-yl)methanone (5l). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (176 mg, 66%): mp 134−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.31 (m, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.38 (s, 1H), 7.52−7.56 (m, 1H), 7.70−7.83 (m, 4H), 8.13 (s, 1H), 10.99 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.5, 115.7, 115.9, 121.0, 124.2, 126.3, 126.7, 129.5, 129.9, 132.2, 132.3, 134.1, 134.2, 136.3, 137.9, 157.2, 164.1, 166.6, 200.1; MS m/z 267 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}FO_2$ 267.0821 [M + H], found 267.0828.

(4-Chlorophenyl)(3-hydroxynaphthalen-2-yl)methanone (5m).[5] Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (189 mg, 67%): mp 134−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, J = 7.6 Hz, 1H), 7.39 (s, 1H), 7.53−7.55 (m, 3H), 7.71−7.74 (m, 4H), 8.12 (s, 1H), 10.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 120.9, 124.3, 126.4, 126.7, 128.9, 129.5, 130.0, 131.0, 136.3, 136.4, 138.0, 138.9, 157.2, 200.4; MS m/z 283 $[MH]^+$.

(4-Bromophenyl)(3-hydroxynaphthalen-2-yl)methanone (5n). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (248 mg, 76%): mp 115−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.38

(m, 2H), 7.52−7.56 (m, 1H), 7.63−7.74 (m, 6H), 8.11 (s, 1H), 11.00 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 120.8, 124.3, 126.4, 126.7, 127.4, 129.6, 130.0, 131.2, 131.9, 136.4, 136.6, 138.0, 157.1, 200.5; MS m/z 327 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}BrO_2$ 327.0021 [M + H], found 327.0018.

4-(3-Hydroxy-2-naphthoyl)benzonitrile (5o).[5] Eluent, petroleum ether−ethyl acetate (10:1). Orange solid (202 mg, 74%): mp 161−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 7.2 Hz, 1H), 7.39 (s, 1H), 7.54−7.58 (m, 1H), 7.71 (d, J = 9.2 Hz, 2H), 7.83−7.88 (m, 4H), 8.02 (s, 1H), 10.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.9, 115.7, 117.9, 120.4, 124.5, 126.4, 126.7, 129.6, 129.8, 130.4, 132.4, 136.6, 138.3, 141.6, 157.1, 200.0; MS m/z 274 $[MH]^+$.

(3-Hydroxynaphthalen-2-yl)(4-(trifluoromethyl)phenyl)-methanone (5p). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (231 mg, 73%): mp 155−157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (t, J = 6.8 Hz, 1H), 7.37 (s, 1H), 7.54 (t, J = 7.2 Hz, 1H), 7.71 (t, J = 7.6 Hz, 2H), 7.83−7.86 (m, 4H), 8.07 (s, 1H), 11.01 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.7, 120.5, 124.4, 125.50, 125.54, 125.57, 125.61, 126.3, 126.7, 129.6, 129.7, 130.2, 136.7, 138.2, 141.0, 157.2, 200.6; MS m/z 317 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{12}F_3O_2$ 317.0789 [M + H], found 317.0788.

(2-Bromo-4-methylphenyl)(3-hydroxynaphthalen-2-yl)-methanone (5q). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (228 mg, 67%): mp 132−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.26 (d, J = 7.2 Hz, 3H), 7.37 (s, 1H), 7.49−7.54 (m, 2H), 7.64−7.69 (m, 2H), 7.90 (s, 1H), 11.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 112.4, 119.4, 120.9, 124.2, 126.4, 126.9, 128.1, 128.9, 129.8, 130.2, 133.9, 136.6, 137.3, 138.4, 142.4, 157.4, 201.8; MS m/z 341 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{14}BrO_2$ 341.0177 [M + H], found 341.0166.

(2-Bromo-4-fluorophenyl)(3-hydroxynaphthalen-2-yl)-methanone (5r). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (248 mg, 72%): mp 139−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21−7.55 (m, 6H), 7.69 (d, J = 6.4 Hz, 2H), 7.85 (d, J = 2.8 Hz, 1H), 11.13−11.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.6, 114.8, 115.0, 120.4, 120.5, 120.7, 120.8, 121.1, 124.3, 126.4, 126.9, 129.7, 130.37, 130.41, 135.7, 137.1, 138.6, 157.2, 161.9, 164.4, 200.7; MS m/z 345 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{11}BrFO_2$ 344.9926 [M + H], found 344.9936.

(3,4-Dimethoxyphenyl)(3-hydroxynaphthalen-2-yl)-methanone (5s). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (219 mg, 71%): mp 119−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (d, J = 4.0 Hz, 3H), 3.99 (d, J = 4.4 Hz, 3H), 6.94−6.96 (m, 1H), 7.30−7.39 (m, 4H), 7.51 (t, J = 7.6 Hz, 1H), 7.69−7.75 (m, 2H), 8.20 (s, 1H), 10.97 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.1, 56.2, 109.9, 112.1, 112.2, 121.4, 124.1, 125.0, 126.3, 126.7, 129.5, 129.6, 130.4, 136.0, 137.6, 149.1, 153.0, 157.1, 199.9; MS m/z 309 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{17}O_4$ 309.1127 [M + H], found 309.1116.

(3-Hydroxynaphthalen-2-yl)(naphthalen-1-yl)methanone (5t). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (197 mg, 66%): mp 124−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.26 (m, 1H), 7.43 (s, 1H), 7.50−7.62 (m, 6H), 7.72 (d, J = 8.8 Hz, 1H), 7.97−8.07 (m, 3H), 8.08 (d, J = 7.2 Hz, 1H), 11.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.4, 122.2, 124.1, 124.5, 125.3, 126.3, 126.79, 126.82, 127.1, 127.5, 128.6, 129.7, 130.1, 130.6, 131.3, 133.7, 135.7, 137.5, 138.4, 157.6, 204.0; MS m/z 299 $[MH]^+$; HRMS (ESI) calcd for $C_{21}H_{15}O_2$ 299.1072 [M + H], found 299.1076.

(3-Hydroxynaphthalen-2-yl)(thiophen-2-yl)methanone (5u). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (165 mg, 65%): mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24−7.27 (m, 1H), 7.36 (t, J = 8.2 Hz, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.81−7.84 (m, 3H), 8.50 (s, 1H), 10.64 (d, J = 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 112.4, 121.7, 124.2, 126.4, 126.9, 128.2, 129.5, 129.7, 134.7, 135.3, 137.6, 142.5, 156.5, 191.3; MS m/z 255 $[MH]^+$; HRMS (ESI) calcd for $C_{15}H_{11}O_2S$ 255.0480 [M + H], found 255.0477.

1-(3-Hydroxynaphthalen-2-yl)-2-phenylethanone (5v). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (176 mg, 67%): mp 133−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (s, 2H), 7.30−7.40 (m, 7H), 7.51−7.55 (m, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 8.51 (s, 1H), 11.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.4, 112.5, 120.7, 124.1, 126.3, 126.8, 127.3, 128.9, 129.48, 129.52, 129.9, 133.4, 133.9, 138.2, 157.4, 204.2; MS m/z 263 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_2$ 263.1072 [M + H], found 263.1070.

1-(3-Hydroxynaphthalen-2-yl)-3-phenylpropan-1-one (5w). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (199 mg, 72%): mp 92−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.13 (t, J = 8.0 Hz, 2H), 3.44 (t, J = 7.4 Hz, 2H), 7.28−7.43 (m, 7H), 7.52 (t, J = 7.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.4 Hz, 1H), 8.24 (s, 1H), 11.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.0, 40.3, 112.3, 120.8, 124.1, 126.3, 126.5, 126.8, 128.6, 128.8, 129.4, 129.7, 132.6, 138.0, 140.8, 157.1, 205.6; MS m/z 277 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{17}O_2$ 277.1229 [M + H], found 277.1209.

(2-Bromophenyl)(3-hydroxy-6-methylnaphthalen-2-yl)-methanone (5x). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (231 mg, 68%): mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (d, J = 2.8 Hz, 3H), 7.12 (d, J = 8.4 Hz, 1H), 7.27 (s, 1H), 7.39−7.56 (m, 5H), 7.71−7.79 (m, 1H), 7.80 (s, 1H), 11.27 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 111.7, 119.4, 120.0, 125.3, 126.8, 127.4, 128.8, 129.6, 131.5, 133.4, 137.0, 138.9, 139.6, 140.9, 157.6, 201.5; MS m/z 341 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{14}BrO_2$ 341.0177 [M + H], found 341.0179.

(2-Bromophenyl)(6-fluoro-3-hydroxynaphthalen-2-yl)-methanone (5y). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (227 mg, 66%): mp 131−133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (t, J = 8.0 Hz, 1H), 7.05 (d, J = 2.0 Hz, 2H), 7.27−7.50 (m, 3H), 7.64−7.73 (m, 2H), 7.83 (s, 1H), 11.32 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.4, 109.6, 111.97, 112.03, 115.0, 115.2, 119.4, 120.09, 120.11, 124.0, 127.4, 128.8, 131.7, 132.6, 132.7, 133.4, 137.2, 139.3, 139.8, 139.9, 158.2, 162.4, 164.9, 201.4; MS m/z 345 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{11}BrFO_2$ 344.9926 [M + H], found 344.9938.

(2-Bromo-4-methylphenyl)(3-hydroxy-6-methylnaphthalen-2-yl)methanone (5z). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (262 mg, 74%): mp 108−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43−2.47 (m, 6H), 7.09−7.11 (m, 1H), 7.26 (s, 3H), 7.44 (s, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.84 (d, J = 2.4 Hz, 1H), 11.34−11.35 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 22.2, 111.7, 119.4, 120.2, 125.28, 125.30, 126.7, 128.1, 128.9, 129.6, 133.8, 136.7, 137.1, 138.8, 140.8, 142.3, 157.6, 201.7; MS m/z 355 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{16}BrO_2$ 355.0333 [M + H], found 355.0334.

(2-Bromo-4-methylphenyl)(6-fluoro-3-hydroxynaphthalen-2-yl)methanone (5aa). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (261 mg, 73%): mp 121−123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.03−7.05 (m, 1H), 7.25−7.27 (m, 4H), 7.53 (s, 1H), 7.62−7.66 (m, 1H), 7.86 (s, 1H), 11.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 109.3, 109.5, 111.86, 111.92, 114.9, 115.1, 119.3, 120.28, 120.30, 124.0, 128.1, 128.8, 132.6, 132.7, 133.9, 136.4, 137.2, 139.7, 139.8, 142.5, 158.3, 162.3, 164.8, 201.6; MS m/z 359 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{13}BrFO_2$ 359.0083 [M + H], found 359.0099.

(2-Bromo-4-fluorophenyl)(3-hydroxy-6-methylnaphthalen-2-yl)methanone (5bb). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (240 mg, 67%): mp 115−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 7.11−7.21 (m, 2H), 7.25 (s, 1H), 7.37−7.46 (m, 3H), 7.55−7.57 (m, 1H), 7.79 (s, 1H), 11.20 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 111.8, 114.7, 114.9, 120.0, 120.4, 120.5, 120.8, 121.0, 125.30, 125.32, 126.9, 129.6, 130.4, 130.5, 135.80, 135.84, 136.9, 138.9, 141.0, 157.5, 161.8, 164.3, 200.5; MS m/z 359 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{13}BrFO_2$ 359.0083 [M + H], found 359.0086.

(2-Bromo-4-fluorophenyl)(6-fluoro-3-hydroxynaphthalen-2-yl)methanone (5cc). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (235 mg, 65%): mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03−7.28 (m, 4H), 7.39−7.48 (m, 2H), 7.65−7.82 (m, 1H), 7.824 (s, 1H), 11.22−11.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.4, 109.6, 112.08, 112.13, 114.8, 115.06, 115.11, 115.4, 120.1, 120.35, 120.43, 120.9, 121.1, 124.0, 130.3, 130.4, 132.6, 132.7, 135.6, 137.0, 139.9, 140.0, 158.1, 161.9, 162.4, 164.4, 164.9, 200.5; MS m/z 363

[MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{10}BrF_2O_2$ 362.9832 [M + H], found 362.9833.

(2-Bromo-4,6-dimethoxyphenyl)(3-hydroxynaphthalen-2-yl)methanone (5dd). Eluent, petroleum ether−ethyl acetate (5:1). Yellow solid (251 mg, 65%): mp 175−177 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.88 (s, 3H), 6.54 (d, J = 2.0 Hz, 1H), 6.81 (d, J = 2.0 Hz, 1H), 7.27 (t, J = 5.4 Hz, 1H), 7.34 (s, 1H), 7.50−7.52 (m, 1H), 7.67−7.70 (m, 2H), 7.90 (s, 1H), 11.29 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.8, 56.1, 98.3, 109.2, 112.1, 120.5, 121.8, 121.9, 123.9, 126.3, 127.2, 129.7, 129.9, 136.2, 138.5, 157.2, 158.6, 162.0, 200.7; MS m/z 387 [MH]$^+$; HRMS (ESI) calcd for $C_{19}H_{16}BrO_4$ 387.0232 [M + H], found 387.0234.

Typical Procedure for the Synthesis of 3-(2-Oxo-2-phenylethyl)-1*H*-isochromen-1-one (6a). To a solution of 2-(4-hydroxy-4-phenylbut-1-ynyl)benzaldehyde (**3a**, 1 mmol) in acetone (10 mL) was added Jones reagent (3 mmol), and the resulting mixture was stirred at 0 °C for 10 min. The resulting mixture was quenched with isopropanol and filtered, and the filtrate was concentrated under a vacuum. The residue was purified by column chromatography on silica gel by using petroleum ether−ethyl acetate (10:1) as the eluent to give **6a**. **6b**−**6r** were obtained in a similar manner.

3-(2-Oxo-2-phenylethyl)-1*H*-isochromen-1-one (6a). Eluent, petroleum ether−ethyl acetate (10:1). White solid (180 mg, 68%): mp 104−106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.19 (s, 2H), 6.47 (s, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.46−7.51 (m, 3H), 7.59−7.68 (m, 2H), 8.00 (d, J = 8.0 Hz, 2H), 8.25 (d, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1, 106.6, 120.4, 125.5, 128.3, 128.5, 128.9, 129.6, 133.9, 134.9, 136.0, 137.0, 150.9, 162.5, 194.0; MS m/z 265 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{13}O_3$ 265.0864 [M + H], found 265.0866.

3-(2-(2-Fluorophenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6b). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (147 mg, 52%): mp 124−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (s, 2H), 6.46 (s, 1H), 7.14−7.27 (m, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.55−7.57 (m, 1H), 7.69 (t, J = 7.6 Hz, 1H), 7.89−7.93 (m, 1H), 8.25 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.6, 47.7, 106.7, 116.7, 116.9, 120.4, 124.81, 124.84, 125.5, 128.3, 129.6, 131.01, 131.03, 134.9, 135.5, 135.6, 137.0, 150.69, 150.71, 160.8, 162.6, 163.3, 192.17, 192.21; MS m/z 283 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{12}FO_3$ 283.0770 [M + H], found 283.0775.

3-(2-Oxo-2-*m*-tolylethyl)-1*H*-isochromen-1-one (6c). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (183 mg, 66%): mp 136−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 4.18 (s, 2H), 6.45 (s, 1H), 7.36−7.42 (m, 3H), 7.47 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.79−7.81 (m, 2H), 8.25 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 43.1, 106.5, 120.4, 125.5, 125.8, 128.2, 128.8, 129.0, 129.6, 134.6, 134.9, 136.1, 137.0, 138.8, 151.1, 162.5, 194.2; MS m/z 279 [MH]$^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_3$ 279.1021 [M + H], found 279.1012.

3-(2-(3-Fluorophenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6d). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (164 mg, 58%): mp 125−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18 (s, 2H), 6.48 (s, 1H), 7.27−7.52 (m, 4H), 7.68−7.72 (m, 2H), 7.80 (d, J = 7.6 Hz, 1H), 8.26 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.2, 106.8, 115.1, 115.3, 120.4, 120.9, 121.1, 124.31, 124.34, 125.5, 128.4, 129.6, 130.6, 130.7, 135.0, 136.9, 138.0, 150.4, 162.5, 164.2, 192.9; MS m/z 283 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{12}FO_3$ 283.0770 [M + H], found 283.0786.

3-(2-(3-Chlorophenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6e). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (179 mg, 60%): mp 156−158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (s, 2H), 6.47 (s, 1H), 7.38−7.72 (m, 5 H), 7.89 (d, J = 7.6 Hz, 1H), 7.97 (s, 1H), 8.26 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1, 106.8, 120.4, 125.5, 126.6, 128.4, 128.5, 129.6, 130.3, 133.8, 135.0, 135.3, 136.9, 137.5, 150.3, 162.4, 192.9; MS m/z 299 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{12}ClO_3$ 299.0475 [M + H], found 299.0476.

3-(2-(3-Bromophenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6f). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (212 mg, 62%): mp 159−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (s, 2H), 6.47 (s, 1H), 7.37−7.52 (m, 3H), 7.68−7.75 (m, 2H), 7.94 (d, J = 7.2 Hz, 1H), 8.13 (d, J = 1.6 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1, 106.8, 120.4, 123.3, 125.5, 127.1, 128.5, 129.7, 130.5, 131.5, 135.0, 136.7, 136.9, 137.7, 150.3, 162.4, 192.8; MS m/z 343 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{12}BrO_3$ 342.9970 [M + H], found 342.9978.

3-(2-(4-Methoxyphenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6g). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (206 mg, 70%): mp 149−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.86 (s, 3H), 4.13 (s, 2H), 6.44 (s, 1H), 6.94 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.96−7.99 (m, 2H), 8.23 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.8, 55.6, 106.4, 114.0, 120.3, 125.5, 128.2, 129.1, 129.5, 130.9, 134.9, 137.1, 151.3, 162.6, 164.1, 192.5; MS m/z 295 [MH]$^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_4$ 295.0970 [M + H], found 295.0973.

3-(2-Oxo-2-*p*-tolylethyl)-1*H*-isochromen-1-one (6h). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (186 mg, 67%): mp 124−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 4.17 (s, 2H), 6.46 (s, 1H), 7.29 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 7.6 Hz, 1H), 7.48 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.91 (d, J = 8.4 Hz, 2H), 8.26 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 42.9, 106.4, 120.3, 125.4, 128.2, 128.6, 129.5, 133.6, 134.8, 137.0, 144.8, 151.1, 162.5, 193.6; MS m/z 279 [MH]$^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_3$ 279.1021 [M + H], found 279.1028.

3-(2-(4-Fluorophenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6i). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (169 mg, 60%): mp 154−156 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (s, 2H), 6.47 (s, 1H), 7.17 (t, J = 8.4 Hz, 2H), 7.38 (d, J = 7.6 Hz, 1H), 7.47−7.51 (m, 1H), 7.67−7.71 (m, 1H), 8.03−8.06 (m, 2H), 8.25 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.0, 106.7, 116.0, 116.2, 120.3, 125.5, 128.4, 129.6, 131.2, 131.3, 135.0, 136.9, 150.7, 162.5, 164.9, 167.4, 192.5; MS m/z 283 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{12}FO_3$ 283.0770 [M + H], found 283.0761.

3-(2-(4-Chlorophenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6j). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (182 mg, 61%): mp 139−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (s, 2H), 6.47 (s, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.46−7.51 (m, 3H), 7.69 (t, J = 7.6 Hz, 1H), 7.95 (d, J = 8.0 Hz, 2H), 8.26 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1, 106.7, 120.4, 125.5, 128.4, 129.3, 129.6, 129.9, 134.3, 135.0, 136.9, 140.4, 150.5, 162.4, 192.9; MS m/z 299 [MH]$^+$; HRMS (ESI) calcd for $C_{17}H_{12}ClO_3$ 299.0475 [M + H], found 299.0476.

3-(2-(3,4-Dimethoxyphenyl)-2-oxoethyl)-1*H*-isochromen-1-one (6k). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (243 mg, 75%): mp 171−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.83 (s, 3H), 3.86 (s, 3H), 4.10 (s, 2H), 6.41 (s, 1H), 6.83−6.86 (m, 1H), 7.30 (d, J = 7.6 Hz, 1H), 7.38−7.42 (m, 1H), 7.48 (d, J = 1.6 Hz, 1H), 7.58−7.62 (m, 2H), 8.15 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7, 56.0, 56.1, 106.4, 110.1, 110.2, 120.2, 123.5, 125.4, 128.2, 129.1, 129.4, 134.9, 137.0, 149.1, 151.3, 153.8, 162.5, 192.7; MS m/z 325 [MH]$^+$; HRMS (ESI) calcd for $C_{19}H_{17}O_5$ 325.1076 [M + H], found 325.1077.

3-(2-(Naphthalen-1-yl)-2-oxoethyl)-1*H*-isochromen-1-one (6l). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (229 mg, 73%): mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.27 (s, 2H), 6.49 (s, 1H), 7.34−7.65 (m, 7H), 7.86 (d, J = 7.2 Hz, 1H), 8.01 (d, J = 7.2 Hz, 2H), 8.23 (d, J = 8.0 Hz, 1H), 8.74 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 46.1, 106.8, 120.3, 124.4, 125.5, 125.8, 126.8, 128.3, 128.5, 128.6, 128.9, 129.5, 130.3, 133.9, 134.00, 134.03, 134.9, 137.0, 151.1, 162.6, 197.4; MS m/z 315 [MH]$^+$; HRMS (ESI) calcd for $C_{21}H_{15}O_3$ 315.1021 [M + H], found 315.1018.

3-(2-Oxo-3-phenylpropyl)-1*H*-isochromen-1-one (6m). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (172 mg, 62%): mp 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (s, 2H), 3.84 (s, 2H), 6.35 (s, 1H), 7.21−7.36 (m, 6H), 7.48 (t, J = 7.6 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 46.2, 50.1, 106.6, 120.3, 125.5, 127.4, 128.4, 128.9, 129.56, 129.60, 133.2, 134.9, 136.9, 150.4, 162.4, 202.1; MS m/z 279 [MH]$^+$; HRMS (ESI) calcd for $C_{18}H_{15}O_3$ 279.1021 [M + H], found 279.1016.

3-(2-Oxo-4-phenylbutyl)-1*H*-isochromen-1-one (6n). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (175 mg, 60%): mp 114−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92 (s, 4H), 3.58 (s, 2H),

6.34 (s, 1H), 7.17−7.37 (m, 5H), 7.36 (d, J = 8.0 Hz, 1H), 7.49 (t, J = 7,6 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.5, 44.4, 47.3, 106.5, 120.3, 125.5, 126.3, 128.4, 128.6, 129.6, 135.0, 136.9, 140.5, 150.4, 162.4, 203.7; MS m/z 293 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{17}O_3$ 293.1177 [M + H], found 293.1180.

6-Fluoro-3-(2-oxo-2-*m*-tolylethyl)-1*H*-isochromen-1-one (6o). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (198 mg, 67%): mp 136−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 4.18 (s, 2H), 6.42 (s, 1H), 7.00−7.18 (m, 2H), 7.34−7.44 (m, 2H), 7.79 (d, J = 6.8 Hz, 2H), 8.24−8.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 43.0, 106.1, 111.0, 111.3, 116.4, 116.6, 125.7, 127.3, 128.4, 128.8, 128.9, 132.9, 133.0, 134.7, 136.0, 138.8, 152.6, 161.6, 165.4, 168.0, 194.0; MS m/z 297 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{14}FO_3$ 297.0927 [M + H], found 297.0933.

3-(2-(3-Chlorophenyl)-2-oxoethyl)-6-fluoro-1*H*-isochromen-1-one (6p). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (183 mg, 58%): mp 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (s, 2H), 6.43 (s, 1H), 7.05 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 7.20 (td, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 7.6 Hz, 1H), 7.96 (d, J = 1.6 Hz, 1H), 8.27−8.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ δ 43.1, 106.2, 106.3, 111.1, 111.4, 116.6, 116.8, 116.89, 116.90, 126.6, 128.5, 130.3, 133.0, 133.1, 133.9, 135.4, 137.5, 139.6, 151.8, 161.4, 165.5, 168.0, 192.5; MS m/z 317 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{11}ClFO_3$ 317.0381 [M + H], found 317.0379.

6-Methyl-3-(2-oxo-2-*p*-tolylethyl)-1*H*-isochromen-1-one (6q). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (193 mg, 66%): mp 118−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.43 (s, 3H), 4.13 (s, 2H), 6.37 (s, 1H), 7.13 (s, 1H), 7.27 (d, J = 7.2 Hz, 3H), 7.89 (d, J = 8.0 Hz, 2H), 8.11 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 21.9, 43.0, 106.4, 117.9, 125.5, 128.7, 129.1, 129.15, 129.24, 129.5, 129.6, 133.6, 137.2, 144.8, 146.0, 151.2, 162.6, 193.7; MS m/z 293 $[MH]^+$; HRMS (ESI) calcd for $C_{19}H_{17}O_3$ 293.1177 [M + H], found 293.1181.

3-(2-(4-Chlorophenyl)-2-oxoethyl)-6-methyl-1*H*-isochromen-1-one (6r). Eluent, petroleum ether−ethyl acetate (10:1). Yellow solid (187 mg, 60%): mp 125−127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 4.13 (s, 2H), 6.38 (s, 1H), 7.14 (s, 1H), 7.26−7.29 (m, 1H), 7.44 (d, J = 7.6 Hz, 2H), 7.93 (d, J = 9.2 Hz, 2H), 8.11 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 43.1, 106.6, 117.9, 125.5, 128.8, 129.2, 129.5, 129.7, 129.9, 131.0, 134.3, 137.0, 140.3, 146.1, 150.5, 162.5, 193.0; MS m/z 313 $[MH]^+$; HRMS (ESI) calcd for $C_{18}H_{14}ClO_3$ 313.0631 [M + H], found 313.0626.

Typical Procedure for the Synthesis of (2-Bromo-4,6-dihydroxyphenyl)(3-hydroxy naphthalen-2-yl)methanone (5ee). To a dried round-bottom flask were added (2-bromo-4,6-dimethoxyphenyl)(3-hydroxy naphthalen-2-yl)methanone (**5dd**, 0.5 mmol) and CH_2Cl_2 (5 mL). The flask was purged with nitrogen. BBr_3 (0.75 mmol) in CH_2Cl_2 was then added dropwise to the mixture. The mixture was allowed to stir at room temperature for 12 h. The reaction was quenched with water and extracted with ethyl acetate (5 mL × 3). The combined organic phases were dried, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on silica gel by using petroleum ether−ethyl acetate (3:1) as the eluent to afford **5ee**.

(2-Bromo-4,6-dihydroxyphenyl)(3-hydroxynaphthalen-2-yl)-methanone (5ee). Eluent, petroleum ether−ethyl acetate (3:1). Yellow solid (125 mg, 70%): mp 158−160 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 6.59 (d, J = 1.6 Hz, 1H), 6.78 (d, J = 1.6 Hz, 1H), 7.29−7.35 (m, 2H), 7.55 (t, J = 7.6 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 8.18 (s, 1H), 9.14 (s, 1H), 9.23 (s, 1H), 11.34 (s, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 102.4, 111.3, 111.6, 119.8, 122.1, 124.0, 126.1, 127.3, 129.7, 129.9, 136.4, 138.4, 156.6, 157.2, 160.1, 201.4; MS m/z 359 $[MH]^+$; HRMS (ESI) calcd for $C_{17}H_{12}BrO_4$ 358.9919 [M + H], found 358.9926.

Typical Procedure for the Synthesis of 1,3-Dihydroxy-12*H*-benzo[*b*]xanthen-12-one (7). To a flask containing (2-bromo-4,6-dihydroxyphenyl)(3-hydroxynaphthalen-2-yl) methanone (**5ee**, 0.2 mmol) in CH_3CN (2 mL) was added K_2CO_3 (0.4 mmol). After the mixture was stirred at 80 °C for 2 h, the reaction was quenched with aqueous solution of NH_4Cl and extracted with ethyl acetate (5 mL × 3). The combined organic layers were washed with H_2O and brine, and then dried over anhydrous Na_2SO_4 and concentrated under a vacuum. The residue was purified by chromatography on silica gel by using petroleum ether−ethyl acetate (3:1) as the eluent to afford **7**.

1,3-Dihydroxy-12*H*-benzo[*b*]xanthen-12-one (7).[15] Eluent, petroleum ether−ethyl acetate (3:1). Yellow solid (51 mg, 91%): mp 270−272 °C (283−285 °C);[15] ^{1}H NMR (400 MHz, acetone-d_6) δ 6.25 (d, J = 2.0 Hz, 1H), 6.42 (d, J = 1.6 Hz, 1H), 7.56 (t, J = 7.2 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.93 (s, 1H), 8.01 (d, J = 8.4 Hz, 1H), 8.17 (d, J = 8.4 Hz, 1H), 8.80 (s, 1H), 9.95 (s, 1H), 12.96 (s, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 94.18, 94.23, 97.68, 97.73, 113.2, 120.2, 125.8, 127.16, 127.23, 129.3, 129.6, 129.7, 136.9, 151.8, 158.4, 164.4, 166.1, 180.9; MS m/z 279 $[MH]^+$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra, and the X-ray crystal structure of **5l**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: xuesen.fan@htu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the Natural Science Foundation of China (21272058, 21172057), RFDP (20114104110005), PCSIRT (IRT 1061), and 2012IRTSTHN006 for financial support.

■ REFERENCES

(1) Malkov, A. V.; Westwater, M.-M.; Gutnov, A.; Ramírez-López, P.; Friscourt, F.; Kadlčíková, A.; Hodačová, J.; Rankovic, Z.; Kotora, M.; Kočovský, P. *Tetrahedron* **2008**, *64*, 11335.

(2) Krause, N.; Hashmi, A. S. K. *Modern Allene Chemistry*; Wiley: Weinheim, 2004; p 3.

(3) Zhang, L.; Zhang, J. Y. *J. Comb. Chem.* **2006**, *8*, 361.

(4) Koch, S. S. C.; Dardashti, L. J.; Hebert, J. J.; White, S. K.; Croston, G. E.; Flatten, K. S.; Heyman, R. A.; Nadzan, A. M. *J. Med. Chem.* **1996**, *39*, 3229.

(5) Li, X. L.; Hewgley, J. B.; Mulrooney, C. A.; Yang, J.; Kozlowski, M. C. *J. Org. Chem.* **2003**, *68*, 5500.

(6) Lucas, S.; Heim, M.; Antes, I.; Ries, C.; Schewe, K. E.; Bisi, A.; Gobbi, S.; Hartmann, R. W. *J. Med. Chem.* **2008**, *51*, 6138.

(7) Murashige, R.; Hayashi, Y.; Ohmori, S.; Torii, A.; Aizu, Y.; Muto, Y.; Murai, Y.; Oda, Y.; Hashimoto, M. *Tetrahedron* **2011**, *67*, 641.

(8) Park, K. K.; Jeong, J. *Tetrahedron* **2005**, *61*, 545.

(9) (a) Hauser, F. M.; Baghdanov, V. M. *J. Org. Chem.* **1988**, *53*, 4676. (b) Subramanian, V.; Batchu, V. R.; Barange, D.; Pal, M. *J. Org. Chem.* **2005**, *70*, 4778. (c) Peuchamaur, M.; Lisowski, V.; Gandreuil, C.; Maillard, L. T.; Martinez, J.; Hernandez, J.-F. *J. Org. Chem.* **2009**, *74*, 4158.

(10) (a) Agata, N.; Nogi, H.; Milhollen, M.; Kharbanda, S.; Kufe, D. *Cancer Res.* **2004**, *64*, 8512. (b) Pochet, L.; Frédérick, R.; Masereel, B. *Curr. Pharm. Des.* **2004**, *10*, 3781.

(11) (a) Matsuda, H.; Shimoda, H.; Yoshikawa, M. *Bioorg. Med. Chem.* **1999**, *7*, 1445. (b) Heynekamp, J. J.; Hunsaker, L. A.; Vander Jagt, T. A.; Deck, L. M.; Vander Jagt, D. L. *BMC Chem. Biol.* **2006**, *6*, 1. (c) Heynekamp, J. J.; Hunsaker, L. A.; Vander Jagt, T. A.; Royer, R. E.; Deck, L. M.; Vander Jagt, D. L. *Bioorg. Med. Chem.* **2008**, *16*, 5285. (d) Ma, S. M.; Zhan, J.; Xie, X.; Watanabe, K.; Tang, Y.; Zhang, W. *J. Am. Chem. Soc.* **2008**, *130*, 38. (e) Zhou, H.; Li, Y.; Tang, Y. *Nat. Prod. Rep.* **2010**, *27*, 839.

(12) (a) Cherry, K.; Parrain, J.-L.; Thibonnet, J.; Duchêne, A.; Abarbri, M. *J. Org. Chem.* **2005**, *70*, 6669. (b) Kajita, Y.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2008**, *130*, 17226. (c) García-Fortanet, J.; Debergh, J. R.; De Brabander, J. K. *Org. Lett.* **2005**, *7*, 685. (d) Özcan, S.; Balci, M. *Tetrahedron* **2008**, *64*, 5531. (e) De Angelis, M.; Stossi, F.; Waibel, M.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A. *Bioorg. Med. Chem.* **2005**, *13*, 6529. (f) Le Bras, G.; Hamze, A.; Messaoudi, S.; Provot, O.; Le Calvez, P.-B.; Brion, J.-D.; Alami, M. *Synthesis* **2008**, 1607. (g) Sperança, A.; Godoi, B.; Pinton, S.; Back, D. F.; Menezes, P. H.; Zeni, G. *J. Org. Chem.* **2011**, *76*, 6789. (h) Guo, X. X. *J. Org. Chem.* **2013**, *78*, 1660. (i) Kavala, V.; Wang, C. C.; Barange, D. K.; Kuo, C. W.; Lei, P. M.; Yao, C. F. *J. Org. Chem.* **2012**, *77*, 5022. (j) Cai, S. J.; Wang, F.; Xi, C. J. *J. Org. Chem.* **2012**, *77*, 2331. (k) Ge, Z. Y.; Fei, X. D.; Tang, T.; Zhu, Y. M.; Shen, J. K. *J. Org. Chem.* **2012**, *77*, 5736. (l) Chen, P. Y.; Huang, K. S.; Tsai, C. C.; Wang, T. P.; Wang, E. C. *Org. Lett.* **2012**, *14*, 4930. (m) Fan, X. S.; He, Y.; Cui, L. Y.; Guo, S. H.; Wang, J. J.; Zhang, X. Y. *Eur. J. Org. Chem.* **2012**, 673.

(13) Uchiyama, M.; Ozawa, H.; Takuma, K.; Matsumoto, Y.; Yonehara, M.; Hiroya, K.; Sakamoto, K. *Org. Lett.* **2006**, *8*, 5517.

(14) (a) Marshall, J. A.; Wang, X.-J. *J. Org. Chem.* **1992**, *57*, 3387. (b) Ma, D.; Yu, Y.; Lu, X. *J. Org. Chem.* **1989**, *54*, 1105.

(15) Liu, Y.; Ma, L.; Chen, W.-H.; Wang, B.; Xu, Z.-L. *Bioorg. Med. Chem.* **2007**, *15*, 2810.

(16) Cho, H.-J.; Jung, M.-J.; Woo, S.; Kim, J.; Lee, E.-S.; Kwon, Y.; Na, Y. *Bioorg. Med. Chem.* **2010**, *18*, 1010.