One-pot synthesis of furocoumarins *via* sequential Pd/Cu-catalyzed alkynylation and intramolecular hydroalkoxylation†

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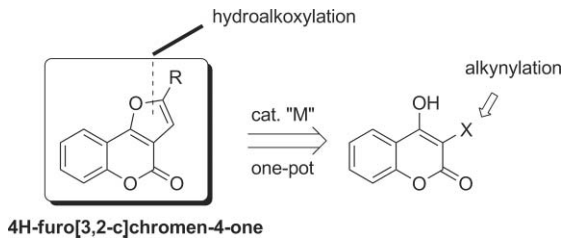
A novel and rapid assembly of an interesting class of furocoumarins-4*H*-furo[3,2-*c*]chromen-4-ones has been successfully achieved using one-pot sequential coupling/cyclization strategy with easily available starting materials 3-bromo-4-acetoxycoumarins and terminal alkynes. The key synthesis involves Pd/Cu-catalyzed alkynylation with *in situ* prepared dialkynylzincs followed by intramolecular hydroalkoxylation.

Introduction

Coumarins are an extremely important family of heterocyclic compounds owing to their presence in a large variety of biologically active substances and their use as valuable agents for pharmaceuticals and fine chemicals.[1] Over the past several decades, synthesis and screening of coumarin compounds for drug discovery has been a vital subject of constant interest in organic and medicinal chemistry.[2] Furocoumarins that contain a common 4*H*-furo[3,2-*c*]chromen-4-one scaffold represent a promising class of synthetic targets because of their noticeable biological properties.[3] In the last few years, there have been many efforts to develop new approaches for synthesis of the related scaffolds.[4,5] Among them, one-pot synthesis of furocoumarins has proved to be one of the most attractive methods, however, only a limited number of reports are currently known.[5] Successful examples including cascade addition/cyclization/oxidation of 3-alkynyl-chromones,[5a,b] propargylation/cyclization of 4-hydroxycoumarins,[5c,d] and Sonogashira-acetylide coupling/demethylation/cyclization of 3-iodo-4-methoxy-coumarin,[5e] but some of these syntheses suffered from low overall yields or relatively poorer substrate availability. Methods for the rapid preparation of furocoumarin derivatives with high reaction efficiency and broad generality are still desired. Herein, we wish to report our efforts on the development of a new and efficient synthetic approach for one-pot synthesis of substituted furocoumarins.

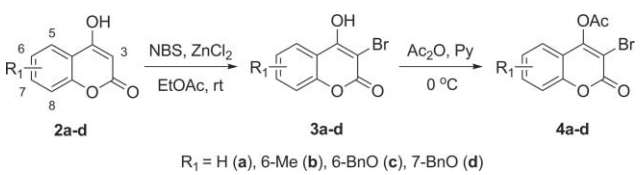
Previously, we have succeeded on straightforward syntheses of chromeno[3,4-*b*]pyrrol-4(3*H*)-one derivatives (pyrrolocoumarins) by palladium-catalyzed sequential coupling/cyclization reactions.[6] The key strategy relies on creation of a pyrrole ring through palladium-catalyzed intramolecular hydroamination of related acetylenic aminocoumarins. In considering the 4*H*-furo[3,2-*c*]chromen-4-one (**1**) framework, we envisioned that the similar construction of a furan ring might be subsequently achieved in one-pot *via* intramolecular hydroalkoxylation[7] after the corresponding alkynylation of 3-halo-4-hydroxycoumarin in the presence of same transition-metal catalyst such as palladium or copper (Scheme 1).



Scheme 1 New strategy for synthesis of 4*H*-furo[3,2-*c*]chromen-4-one.

Results and discussion

To begin addressing the above hypothesis, we first sought to find a mild reaction which would allow the easy preparation of key intermediate 3-halo-4-hydroxycoumarins. It has been reported that 3-bromo-4-hydroxycoumarin could be generated by treatment of commercially available 4-hydroxycoumarin with NBS using $Mg(ClO_4)_2$ as a Lewis acid.[8] However, perchlorate salts are potentially explosive and need to be handled with great care. For safety concern, we turned our attention to other Lewis acids which might catalyze the C-3 bromination of 4-hydroxycoumarins in a mild and practical way. Fortunately, after several attempts, when $ZnCl_2$ combined with NBS in EtOAc was employed, the reaction underwent smoothly and gave the desired product 3-bromo-4-hydroxycoumarin **3a** with a satisfactory yield of 81% (Scheme 2).



Scheme 2 Improved synthesis of 3-bromo-4-hydroxycoumarins and their derivatives.

With the key intermediate 3-bromo-4-hydroxycoumarin **3a** in hand, we then investigated the potential of cascade

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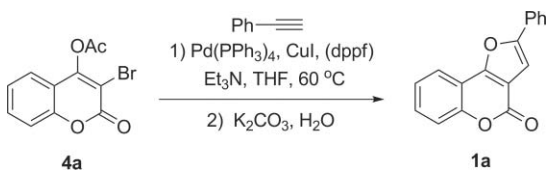
coupling/cyclization, as proposed in Scheme 1, to construct the designed furocoumarins (4*H*-furo[3,2-*c*]chromen-4-ones). Cross-coupling of 3-bromo-4-hydroxycoumarin **3a** with phenylacetylene was initially examined under Sonogashira[9] conditions ($Pd(PPh_3)_4$, CuI, Et_3N, THF, 60 °C). However, the result was disappointing. Considerable amount of the debromo coumarin formation was found, and neither the desired cross-coupling product nor furocoumarin was isolated. It appeared that the unprotected electron-rich hydroxy group at the neighboring C-4 position is responsible for this undesired C-3 debromination. To address the issue, we decided to introduce an electron-withdrawing acetyl group to the hydroxy oxygen. The advantages of this introduction could be considered as follows: 1) the electron density on the oxygen can be largely lowered; 2) further activation of the C–Br bond by two electron-withdrawing groups *ortho*-acetoxy and -ester carbonyl to enable smooth alkynylation might be expected; 3) removal of the acetyl should be easily accomplished in base conditions, making it feasible to proceed intramolecular alkyne hydroalkoxylation. Accordingly, the 3-bromo-4-acetoxycoumarins were readily produced by further treatment of the C-3 bromination products 3-bromo-4-hydroxycoumarins **3** with Ac_2O in the presence of pyridine in one-pot (Scheme 2).

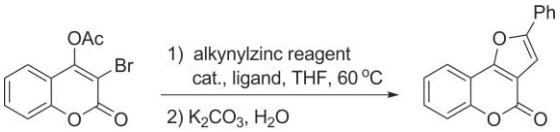
Next, the reaction of 3-bromo-4-acetoxycoumarin **4a** with phenylacetylene was examined. In contrast to the case of 3-bromo-4-hydroxycoumarin, the expected furocoumarin product **1a** was observed, however, the yield was low (8%). To our delight, the use of 1,1′-bis(diphenylphosphino)ferrocene (dppf) as additive was found to be helpful, the reaction gave the desired furocoumarin in 29% yield together with 14% of cross-coupling product in 5 h. These results indicate that the expected cascade coupling/cyclization process occurs and its incompletion may account for the rather difficult hydrolysis of the acetyl under mild Sonogashira conditions. Indeed, when an additional hydrolysis procedure (K_2CO_3, H_2O) was employed in one-pot, a much higher yield (51%) of furocoumarin **1a** was obtained (Scheme 3). Despite this improvement, the Sonogashira alkynylation appeared to not be satisfactory.



Scheme 3 Synthesis of furocoumarin *via* Sonogashira coupling approach.

In order to achieve better efficiency in the reaction of cross-coupling step, we envisioned to investigate other alternative strategies such as Negishi cross-coupling.[10] Recently, the use of preformed metallated alkynes especially alkynylzincs for efficient alkynylation has proved promising.[11] Unfortunately, when the routine made phenylethynylzinc chloride and bromide were attempted to react with 3-bromo-4-acetoxycoumarin **4a** under the above same reaction conditions, the desired furocoumarin **1a** was not obtained in more than 15% yield (Table 1, entries 1 and 2). In conjunction with our recent interests in asymmetric alkynylzinc addition to aldehydes,[12] we were curious as to whether the reactive species methylalkynylzinc and dialkynylzinc could be applied to the expected alkynylation. These zinc acetylides

Table 1 Attempts on using alkynylzinc reagents for cross-coupling[a]



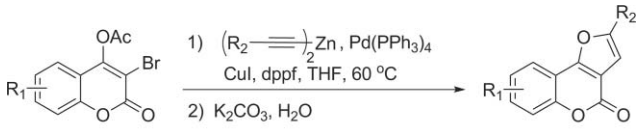
Entry	Ph—≡—ZnX	$Pd(PPh_3)_4$ (mol%)	CuI (mol%)	Ligand	Yield (%)[b]
1	Ph—≡—ZnCl	15	15	dppf	trace
2	Ph—≡—ZnBr	15	15	dppf	15
3	Ph—≡—ZnMe	15	15	dppf	25
4	(Ph—≡—)$_2$Zn	15	15	dppf	81
5	(Ph—≡—)$_2$Zn	10	10	dppf	75
6	(Ph—≡—)$_2$Zn	15	15	None	38
7	(Ph—≡—)$_2$Zn	15	—	dppf	19

[a] The cross-coupling reaction was carried out with **4a** (0.2 mmol), indicated phenylethynylzinc reagent (0.3 mmol) in the presence of $Pd(PPh_3)_4$ (0.03 mmol), CuI (0.03 mmol), and indicated ligand (0.03 mmol) in distilled THF (5 mL). [b] Isolated yield.

can be prepared *in situ* by direct metallation of 1-alkynes with Me_2Zn.[13] To our knowledge, their reactivity in cross-coupling reactions has been far less explored.[14] In 2000, efficient cross-couplings of corresponding alkynylzinc reagents with unsaturated organotellurium compounds were described.[14c] In our case, when methyl(phenylethynyl)zinc was employed by the catalysis of $Pd(PPh_3)_4$/CuI/dppf, the reaction afforded **1a** in 25% yield (entry 3) together with 34% yield of competitive methylation product. Gratifyingly, di(phenylethynyl)zinc was found very effective in the related transformation, generating the cascade coupling/cyclization product **1a** in good yield (81%) under the same one-pot conditions (entry 4). When the reaction was carried out in the absence of dppf, only 38% yield was afforded (entry 6). Our further efforts on ligand screening using (*o*-tolyl)$_3$P, 1,3-bis(diphenylphosphino)propane (dppp), Xanphos and (*R*)-BINAP did not gave better results (< 50% yield). A slight decrease of the reaction yield (75%) was observed with lowered catalyst loading of $Pd(PPh_3)_4$ and CuI (entry 5). Notably, the reaction catalyzed without CuI only provided 19% of **1a**, suggesting its important role in the process (entry 7).

Consequently, the one-pot cascade coupling/cyclization procedure for the synthesis of diverse substituted furocoumarins was examined with 3-bromo-4-acetoxycoumarins **4** and a range of dialkynylzincs prepared from the corresponding 1-alkynes using the optimal conditions in Table 1, entry 4, the results are summarized in Table 2. It was found that both aromatic and aliphatic alkynes could be typically employed in the reaction

Table 2 Synthesis of diverse substituted furocoumarins

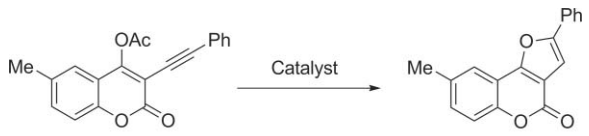


4 1

Entry[a]	R_1	R_2	1	Yield (%)[b]
1	H	C_6H_5	**1a**	81
2	H	4-*t*-BuC_6H_4	**1b**	66
3	H	4-MeOC_6H_4	**1c**	91
4	H	3,5-(MeO)$_2C_6H_3$	**1d**	76
5	H	3,4,5-(MeO)$_3C_6H_2$	**1e**	54
6	H	*t*-Bu	**1f**	65
7	H	*n*-Bu	**1g**	64
8	H	1-Cyclohexenyl	**1h**	53
9	6-Me	C_6H_5	**1i**	96
10	7-BnO	C_6H_5	**1j**	88
11	6-BnO	4-*t*-BuC_6H_4	**1k**	67
12	6-Me	4-*t*-BuC_6H_4	**1l**	60
13	7-BnO	4-FC_6H_4	**1m**	51

[a] The cross-coupling reaction was carried out with alkyne (0.6 mmol), $ZnMe_2$ (1.2 M in toluene, 0.25 mL, 0.3 mmol), and **4** (0.2 mmol) in the presence of $Pd(PPh_3)_4$ (0.03 mmol), CuI (0.03 mmol), dppf (0.03 mmol) in distilled THF (5 mL). [b] Isolated yield.

Table 3 Cyclization of coupling intermediate



5 1i

Entry[a]	Conditions	Time/h	Yield[b]
1	K_2CO_3/H_2O, THF, reflux	24	0
2	15 mol% $Pd(PPh_3)_4$, K_2CO_3/H_2O, THF, reflux	18	45
3	15 mol% CuI, K_2CO_3/H_2O, THF, reflux	18	91
4	5 mol% CuI, K_2CO_3/H_2O, THF, reflux	36	46
5	15% $InCl_3$, K_2CO_3/H_2O, THF, reflux	36	39

[a] Reaction was performed with **5** in 0.1 mmol scale in distilled THF (5 mL). [b] Isolated yield.

sequence. Regardless of the substituent pattern and the electronic property of R_2, the desired furocoumarin products could be obtained in moderate to good yields (entries 1–8). Moreover, the reactions with 6- and 7-substituted coumarins were also feasible (entries 9–13).

To gain some preliminary understanding of the step of hydroalkoxylation, we further investigated the cyclization of coupling product **5** under several different reaction conditions (Table 3). A control experiment was performed by treatment with K_2CO_3/H_2O in THF at 60 °C, demonstrating that in the absence of transition-metal catalyst no furocoumarin product **1i** could be observed (entry 1). Indeed, the use of catalytic amount of either $Pd(PPh_3)_4$, or CuI assisted the hydroalkoxylation (entries 2–4). As indicated, CuI appeared to have superior catalytic efficiency, affording the desired product in high yield (91%, entry 3). Thus, we assume at present the actual transformation in the cascade procedure was cooperatively catalyzed by $Pd(PPh_3)_4$ and CuI. Interestingly, $InCl_3$ is also capable of catalyzing the reaction, but was less effective (entry 5).

Conclusion

In summary, a novel and rapid assembly of an interesting class of furocoumarins-4*H*-furo[3,2-*c*]chromen-4-ones has been successfully achieved using one-pot sequential coupling/cyclization strategy with easily available starting materials 3-bromo-4-acetoxycoumarins and 1-alkynes. The cascade transformation relies on palladium/copper-catalyzed alkynylation and intramolecular hydroalkoxylation. The use of *in situ* prepared dialkynylzincs as reactive acetylides in transition-metal catalyzed cross-coupling reactions was rarely reported, our current study provides an important alternative route to form C(sp^2)-C(sp) bond. We anticipate that this approach would be useful for providing a valuable source of new physiologically active coumarin agents. Further research to investigate the utility of current methodology is underway.

Experimental

General procedure for synthesis of 3-bromo-4-acetoxycoumarins (4)

A mixture of 4-hydroxycoumarin compound **2** (1 mmol), NBS (1.1mmol) and $ZnCl_2$ (0.5–1 mmol) in EtOAc (5 mL) was stirred at room temperature until TLC indicated consumption of the starting material **2**. The reaction solution was cooled to 0 °C, then pyridine (1.5 mmol) and acetic anhydride (1.2 mmol) were added, and the stirring was maintained for another 0.5 h. The mixture was diluted with EtOAc, filtered through a short silica gel layer and concentrated under vacuum. The residue was purified by column chromatography (petroleum ether/CH_2Cl_2, 1/1) on silica gel to afford product **4** as white solid.

3-Bromo-4-acetoxycoumarin (4a). 0.5 mmol $ZnCl_2$ was used. 75% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (s, 3H), 7.31–7.65 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 104.7, 115.9, 116.7, 122.6, 124.9, 133.0, 151.7, 157.6, 157.7, 165.3. MS (ESI) *m*/*z*: 305/307 $[M+Na]^+$/$[M+2+Na]^+$. ESI-HRMS calcd for $C_{11}H_7BrNaO_4$ $[M+Na]^+$ 304.9425, found 304.9432.

3-Bromo-4-acetoxy-6-methylcoumarin (4b). 0.5 mmol $ZnCl_2$ was used. 77% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.50 (S, 3H), 7.23–7.41 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 20.9, 104.8, 115.8, 116.7, 122.2, 134.1, 135.0, 150.1, 157.6, 158.0, 165.5. IR (KBr): ν 1790, 1726, 1618, 1570, 1163, 1078, 997, 824 cm^{-1}. MS (ESI) *m*/*z*: 319/321 $[M+Na]^+$/$[M+2+Na]^+$.

3-Bromo-4-acetoxy-6-benzyloxycoumarin (4c). 1.0 mmol $ZnCl_2$ was used. 58% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 5.09 (s, 2H), 6.95 (d, J = 3.0 Hz, 1H), 7.22–7.44 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 70.9, 105.5, 106.8, 116.6, 118.1, 120.9, 127.5, 128.4, 128.7, 135.9, 146.4, 155.6, 157.3, 157.9, 165.2. IR (KBr): ν 1792, 1728, 1570, 1441, 1275, 1165, 1022 cm^{-1}. MS (ESI) *m*/*z*: 411/413 $[M+Na]^+$/$[M+2+Na]^+$.

3-Bromo-4-acetoxy-7-benzyloxycoumarin (4d). 1.0 mmol $ZnCl_2$ was used. 60% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.47 (s, 3H), 5.13 (s, 2H), 6.92–6.97 (m, 2H), 7.37–7.42 (m, 6H);

^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 70.7, 101.2, 101.8, 109.7, 114.0, 123.9, 127.5, 128.5, 128.7, 135.3, 153.7, 157.9, 158.3, 162.7, 165.4. IR (KBr): ν 1774, 1716, 1606, 1367, 1184, 1086 cm^{-1}. MS (ESI) m/z: 411/413 $[M+Na]^+$/$[M+2+Na]^+$.

General procedure for synthesis of furocoumarins (1)

Under nitrogen atmosphere, alkyne (0.6 mmol), freshly distilled THF (5 mL) and $ZnMe_2$ (1.2 M in toluene, 0.25 mL, 0.3 mmol) were successively added into a dry flask. The reaction mixture was stirred at 60 °C for 4 h and then cooled to room temperature. The solution was transferred by cannula under nitrogen into another dry flask charged with 3-bromo-4-acetoxycoumarin **4** (0.2 mmol), $Pd(PPh_3)_4$ (0.03 mmol), dppf (0.03 mmol), CuI (0.03 mmol). The mixture was heated at 60 °C for 6 h. 0.5 mL of degassed saturated aqueous solution of K_2CO_3 was subsequently added and the reaction was stirred at 60 °C overnight. The mixture was cooled to room temperature and diluted with EtOAc, washed with water. The organic layer was filtered through a short silica gel layer, dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by column chromatography (petroleum ether/EtOAc) on silica gel to afford product **1**.

2-Phenyl-4*H*-furo[3,2-*c*]chromen-4-one (1a). 81% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (s, 1H), 7.34–7.95 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 102.5, 112.3, 112.5, 117.2, 120.6, 124.4, 124.5, 128.7, 128.9, 129.0, 130.5, 152.4, 156.4, 156.6, 158.1. IR (KBr): ν 3107, 1736, 1633, 1487, 1425, 1186, 1057,962, 748, 690 cm^{-1}. MS (ESI) m/z: 263 $[M+H]^+$. ESI-HRMS calcd for $C_{17}H_{10}NaO_3$ $[M+Na]^+$ 285.0527, found 285.0533.

2-(4-*tert*-Butylphenyl)-4*H*-furo[3,2-*c*]chromen-4-one (1b). 66% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 7.13 (s, 1H), 7.34–7.97 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 34.8, 102.0, 112.5, 112.8, 117.3, 120.8, 124.4, 124.5, 125.96 (2C), 126.2, 130.5, 152.5, 156.7, 156.9, 158.4. IR (KBr): ν 3113, 2964, 1743, 1626, 1184, 1068, 968, 752 cm^{-1}. MS (ESI) m/z: 319 $[M+H]^+$. ESI-HRMS calcd for $C_{21}H_{19}O_3$ $[M+H]^+$ 319.1334, found 319.1339.

2-(4-Methoxyphenyl)-4*H*-furo[3,2-*c*]chromen-4-one (1c). 91% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H), 6.98 (d, J = 8.7 Hz, 2H), 7.02 (s, 1H), 7.33–7.53 (m, 3H), 7.76 (d, J = 8.7 Hz, 2H), 7.91–7.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 100.9, 112.5, 112.8, 114.4, 117.3, 120.6, 121.7, 124.5, 126.1, 130.3, 152.4, 156.3, 156.7, 158.4, 160.3. IR (KBr): ν 2955, 1747, 1612, 1495, 1265, 1178, 1072, 972, 824, 748 cm^{-1}. MS (ESI) m/z: 263 $[M+Na]^+$. ESI-HRMS calcd for $C_{18}H_{12}NaO_4$ $[M+Na]^+$ 315.0633, found 315.0640.

2-(3,5-Dimethoxyphenyl)-4*H*-furo[3,2-*c*]chromen-4-one (1d). 76% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.83 (s, 6H), 6.43 (s, 1H), 6.86 (s, 1H), 6.87 (s, 1H), 7.08 (s, 1H), 7.31–7.90 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 101.0, 102.6, 103.0, 112.3, 112.5, 117.2, 120.7, 124.5, 130.4, 130.5, 152.5, 156.2, 156.6, 158.0, 161.1. IR (KBr): ν 2922, 1738, 1633, 1597, 1568, 1452, 1205, 1159, 1068, 750 cm^{-1}. MS (ESI) m/z: 323 $[M+H]^+$. ESI-HRMS calcd for $C_{19}H_{15}O_5$ $[M+H]^+$ 323.0919, found 323.0928.

2-(3,4 5-Trimethoxyphenyl)-4*H*-furo[3,2-*c*]chromen-4-one (1e). 54% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.95 (s, 6H), 6.99 (s, 2H), 7.09 (s, 1H), 7.34–7.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 56.3, 61.0, 101.9, 102.4, 112.5, 112.6, 117.4, 120.7, 124.4, 124.5, 130.5, 139.1, 152.5, 153.7, 156.4, 156.6, 158.1. IR (KBr): ν 2943, 1743, 1591, 1497, 1413, 1242, 1126, 754 cm^{-1}. MS (ESI) m/z: 353 $[M+H]^+$. ESI-HRMS calcd for $C_{20}H_{16}NaO_6$ $[M+Na]^+$ 375.0844, found 375.0856.

2-*tert*-Butyl-4*H*-furo[3,2-*c*]chromen-4-one (1f). 65% Yield, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 6.56 (s, 1H), 7.33–7.87 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 33.1, 100.7, 111,2, 113.0, 117.2, 120.6, 124.3, 130.1, 152.3, 156.5, 158.6, 167.7. IR (KBr): ν 2966, 2872, 1741, 1633, 1576, 1502, 1363, 1059, 966, 746 cm^{-1}. MS (ESI) m/z: 243 $[M+H]^+$. ESI-HRMS calcd for $C_{15}H_{14}NaO_3$ $[M+Na]^+$ 265.0840, found 265.0846.

2-Butyl-4*H*-furo[3,2-*c*]chromen-4-one (1g). 64% Yield, brown gum. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, J = 7.5 Hz, 3H), 1.37.1.77 (m, 4H), 2.79 (t, J = 7.5 Hz, 2H), 6.57 (s, 1H), 7.29–7.84 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 22.1, 27.7, 29.6, 103.2, 111.3, 112.9, 117.1, 120.5, 124.3, 130.0, 152.2, 156.4, 158.4, 160.0. IR (KBr): ν 3118, 2953, 2868, 1734, 1628, 1587, 1500, 1161, 966, 756 cm^{-1}. MS (ESI) m/z: 243 $[M+H]^+$. ESI-HRMS calcd for $C_{15}H_{14}NaO_3$ $[M+Na]^+$ 265.0840, found 265.0845.

2-Cyclohexenyl-4*H*-furo[3,2-*c*]chromen-4-one (1h). 53% Yield, white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64–1.84 (m, 4H), 2.25–2.35 (m, 4H), 6.57–6.60 (m, 1H), 6.64 (s, 1H), 7.29–7.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 22.0, 24.6, 25.2, 100.9, 111.8, 112.7, 117.1, 120.6, 124.4, 126.0, 126.6, 130.2, 152.4, 156.1, 157.9, 158.4. IR (KBr): ν 2926, 2852, 1743, 1645, 1630, 1498, 1059, 966, 754 cm^{-1}. MS (ESI) m/z: 267 $[M+H]^+$. ESI-HRMS calcd for $C_{17}H_{14}NaO_3$ $[M+Na]^+$ 289.0840, found 289.0845.

8-Methyl-2-phenyl-4*H*-furo[3,2-*c*]chromen-4-one (1i). 96% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3H), 7.08 (s, 1H), 7.26–7.45 (m, 5H), 7.64 (s, 1H), 7.73–7.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 102.5, 112.25 (2C), 117.0, 120.4, 124.4, 128.8, 128.9, 129.0, 131.6, 134.4, 150.7, 156.3, 156.8, 158.3. IR (KBr): ν 1738, 1637, 1570, 1506, 1488, 1428, 979, 755 cm^{-1}. MS (ESI) m/z: 277 $[M+H]^+$. ESI-HRMS calcd for $C_{18}H_{13}O_3$ $[M+H]^+$ 277.0864, found 277.0866.

7-(Benzyloxy)-2-phenyl-4*H*-furo[3,2-*c*]chromen-4-one (1j). 88% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.13 (s, 2H), 7.00–7.04 (m, 2H), 7.11 (s, 1H), 7.33–7.84 (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.4, 102.4, 106.2, 110.0, 113.4, 121.7, 124.3, 127.5, 128.31 (2C), 128.7, 128.8, 128.9, 128.9, 135.7, 154.1, 155.6, 157.4, 158.5, 160.9. IR (KBr): ν 3099, 2924, 1736, 1628, 1608, 1510, 1439, 1256, 1157, 1105, 1013, 760, 694 cm^{-1}. MS (ESI) m/z: 369 $[M+H]^+$. ESI-HRMS calcd for $C_{24}H_{16}NaO_4$ $[M+Na]^+$ 391.0946, found 391.0947.

8-(Benzyloxy)-2-(4-*tert*-butylphenyl)-4*H*-furo[3,2-c]chromen-4-one (1k). 67% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 5.18 (s, 2H), 7.12 (s, 1H), 7.13 (d, J = 3.0 Hz, 1H), 7.16 (d, J = 3.0 Hz, 1H), 7.36–7.52 (m, 8H), 7.74 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 34.8, 70.8, 102.1, 104.2, 112.7, 113.1, 118.5, 118.9, 124.4, 126.0, 126.2, 127.6, 128.3, 128.7, 136.3, 147.1, 152.5, 155.4, 156.5, 156.9, 158.4. IR (KBr): ν 2960, 1728, 1568, 1495, 1211, 1057, 995, 758, 700 cm^{-1}. MS (ESI) m/z: 425 $[M+H]^+$. ESI-HRMS calcd for $C_{28}H_{24}NaO_4$ $[M+Na]^+$ 447.1572, found 447.1585.

2-(4-*tert*-Butylphenyl)-8-methyl-4*H*-furo[3,2-*c*]chromen-4-one (1l). 60% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 2.48 (S, 3H), 7.12 (s, 1H), 7.32–7.76 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 31.2, 34.8, 102.0, 112.4, 112.5, 117.1, 120.5, 124.4, 125.93 (2C), 126.2, 131.5, 134.4, 150.7, 152.4, 156.7, 158.6. IR (KBr): ν 3109, 2962, 1736, 1633, 1570, 1493, 1182, 980, 916, 822, 768, 555 cm^{-1}. MS (ESI) *m/z*: 333 $[M+H]^+$. ESI-HRMS calcd for $C_{22}H_{21}O_3$ $[M+H]^+$ 333.1490, found 333.1496.

7-(Benzyloxy)-2-(4-fluorophenyl)-4*H*-furo[3,2-*c*]chromen-4-one (1m). 51% Yield, yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.13 (s, 2H), 6.99–7.82 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.4, 102.1, 102.4, 106.2, 110.0, 113.5, 116.1 (d, J = 22.0 Hz), 121.7, 125.4, 126.2 (d, J = 8.1 Hz), 127.5, 128.4, 128.7, 135.7, 154.2, 154.7, 157.4, 158.4, 161.0, 162.9 (d, J = 248.5 Hz). IR (KBr): ν 3111, 2929, 1736, 1628, 1605, 1512, 1497, 1448, 1256, 1232, 1155, 1105, 1011, 833, 700 cm^{-1}. MS (ESI) *m/z*: 387 $[M+H]^+$. ESI-HRMS calcd for $C_{24}H_{16}FO_4$ $[M+H]^+$ 387.1032, found 387.1039.

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