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Graphical Abstract

Synthesis of Furo[3,2-*c*]coumarins *via* I_2/TBHP-mediated Reaction of 4-Hydroxycoumarins with Terminal Alkynes

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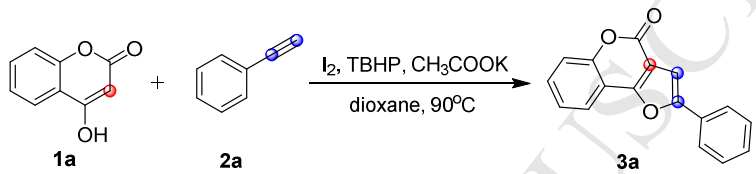

An efficient I_2/TBHP-mediated process for the formation of furo[3,2-*c*]coumarins has been developed. This process for the formation of furo[3,2-*c*]coumarins is quite environmental friendly and atom-economical.

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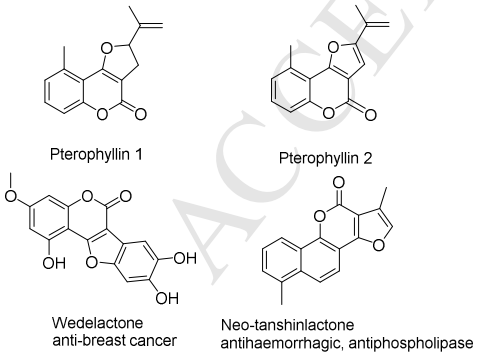
ABSTRACT

An efficient I_2/TBHP-mediated process for the formation of furo[3,2-*c*]coumarins from readily available materials has been developed. This process for the formation of furo[3,2-*c*]coumarins is quite environmental friendly and atom-economical.

1. Introduction

The furocoumarin core is characterized as a significant structure that widely exists in many biologically active natural products,[1] such as pterophyllin, wedelactone, neo-tanshinlactone (Figure 1). Furocoumarin derivatives have been found to possess great interesting biological activities including anti-neurodegenerative diseases, antitumor, anticancer, Na^+, K^+-ATPase inhibitors.[2]

Figure 1. Representative furocoumarin molecules.



Due to its great value, much effort has been devoted to the synthesis of furocoumarin derivatives. The cyclization of alkynylcoumarins catalyzed by transition-metal[3] or iodine[4] is one of the most efficient among these methods. Another alternative approach is sequential coupling/cyclization of terminal alkynes with 3-halo-4-hydroxycoumarins.[5] Lin et al.[6] reported the synthesis of polysubstituted furo[3,2-*c*]coumarins from phosphorus zwitterions and acid chlorides. Foti and Cristina[7] reported the formation of furo[3,2-*c*]coumarins from 4-hydroxycoumarins and double electrophile *α*-haloketones (Scheme 1a). Recently, Chen and co-workers[8] developed a palladium catalyzed C–H functionalization strategy for the construction of furo[3,2-*c*]coumarins. (Scheme 1b). However, these methods suffered from metal contamination, harsh reaction conditions and prefunctionalization of starting materials. Very recently, Hajra and Dey[9] employed 4-hydroxycoumarins with alkynes catalyzed by $FeCl_3/ZnI_2$ to furnish furo[3,2-*c*]coumarins in a convenient and direct synthesis method (Scheme 1b). Herein, we reported a transition-metal free strategy for the synthesis of furo[3,2-*c*]coumarins from 4-hydroxycoumarins and terminal alkynes using I_2/TBHP under aerobic conditions (Scheme 1c). Advantages of this process include the better atom-economy and commercial availability of the starting materials. Futhermore, molecular iodine is an environmental friendly, cheap and easy storage solid reagent. It has been proved that iodine could be a substitute for transtion-metal to catalyze some organic reactions.[10]

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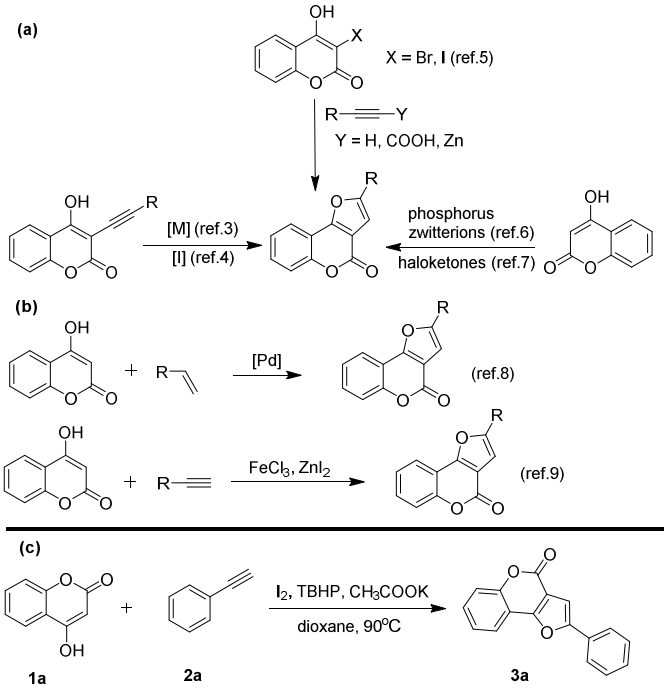
Scheme 1. Representative approaches for synthesis of furo[3,2-*c*]coumarins

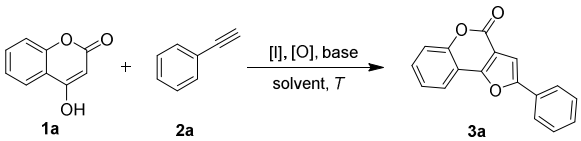


2. Results and Discussion

We began to study the reaction utilizing 4-hydroxycoumarin (**1a**) and phenylacetylene (**2a**) as model substrates to screen the reaction conditions (Table 1). When the reaction was performed at silver/base system,[12e] the target molecule furo[3,2-*c*]coumarin (**3a**) was obtained in a low yield (Table 1, entries 1-2). Gratifyingly, the reaction proceeded smoothly to get the **3a** when [I] (iodine source) was added to the reaction system (Table 1, entries 3-5) and molecule I_2 was the best iodine source affording the compound **3a** in a yield of 73% (Table 1, entry 6). Encouraged by this result, we studied the effect of equivalent of I_2. Regretfully, catalytic amount of I_2 only afforded **3a** in 23% yield and the best equivalent of I_2 was 0.8 equiv (see Supporting Information Table 1, entries 1-6). A series of oxidants were then examined for the reaction, including BQ (benzoquinone), BPO (dibenzoyl peroxide) and O_2. Trace amount of target compound was obtained in the absence of oxidant and TBHP was still the best choice (Table 1, entries 6-10). A screening of base, such as CH_3COONH_4, K_3PO_4, *t*-BuOK, K_2CO_3, Et_3N, DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), proved that CH_3COOK was the optimal base to give **3a** in a yield of 73% (Table 1, entries 11-17). Further switching solvent like DMSO, H_2O, MeCN, dioxane found that the yield of **3a** was slightly improved with the dioxane (Table 1, entries 18-22). Increasing or reducing the temperature had a negative influence on this transformation (see Supporting Information Table 1, entries 7-8). Finally, the optimized reaction conditions were **2a** (0.5 mmol), 3 equiv of **1a**, 0.8 equiv of I_2, 3 equiv of TBHP and 1 equiv of CH_3COOK in 4 mL dioxane at 90 ^oC for 8 h under air atmosphere.

With the optimized conditions in hand, the substrate scope was then examined. The results are summarized in Scheme 2. A series of terminal alkynes with different electronic properties smoothly underwent the reaction, the corresponding compounds were obtained in 30-88% yields (Scheme 2, **3a-n**). Generally, electron-donating substituents on the aromatic ring have positive effect on

Table 1. Optimizing the conditions for the formation of 3a.[a]



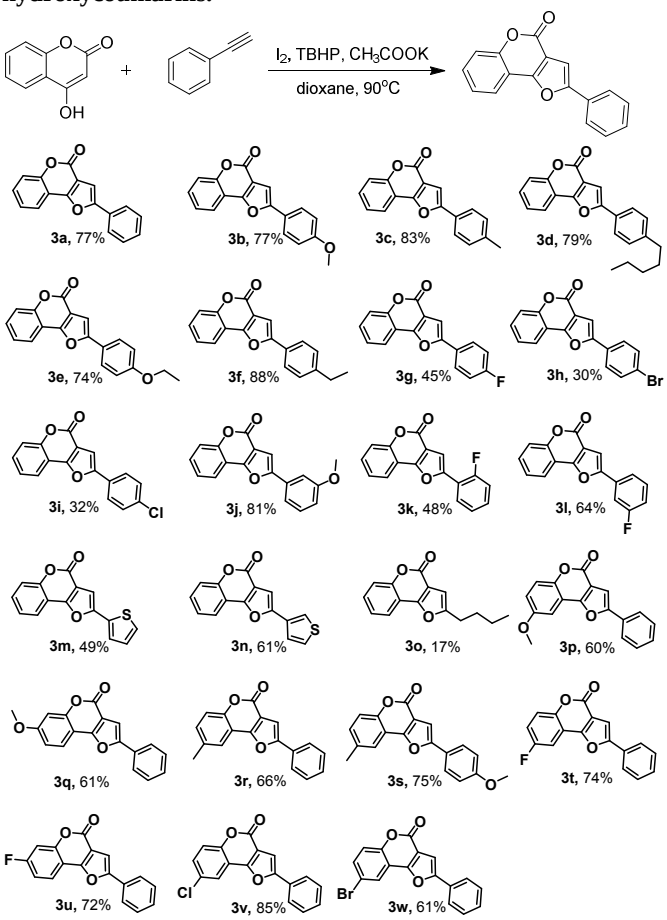
entry	[I]	[O]	base	solvent	yield, %[b]
1	–	AgF	Cs_2CO_3	DMF	trace
2	–	Ag_2CO_3	CH_3CO_2K	DMF	7
3	NH_4I	TBHP	CH_3CO_2K	DCE	–
4	ZnI_2	TBHP	CH_3CO_2K	DCE	21
5	NIS	TBHP	CH_3CO_2K	DCE	trace
6	I_2	TBHP	CH_3CO_2K	DCE	73
7	I_2	–	CH_3CO_2K	DCE	trace
8	I_2	BQ	CH_3CO_2K	DCE	–
9	I_2	BPO	CH_3CO_2K	DCE	62
10	I_2	O_2	CH_3CO_2K	DCE	–
11	I_2	TBHP	$CH_3CO_2NH_4$	DCE	47
12	I_2	TBHP	K_3PO_4	DCE	–
13	I_2	TBHP	*t*-BuOK	DCE	49
14	I_2	TBHP	K_2CO_3	DCE	8
15	I_2	TBHP	NEt_3	DCE	60
16	I_2	TBHP	DBU	DCE	68
17	I_2	TBHP	–	DCE	30
18	I_2	TBHP	CH_3CO_2K	H_2O	20
19	I_2	TBHP	CH_3CO_2K	DMSO	–
20	I_2	TBHP	CH_3CO_2K	MeCN	19
21	I_2	TBHP	CH_3CO_2K	H_2O/DCE 1:1	15
22	I_2	TBHP	CH_3CO_2K	Dioxane	77

[a]Reaction conditions: **1a** (1.5 mmol), **2a** (0.5 mmol), [I] (0.4 mmol), [O] (1.5 mmol), base (0.5 mmol) and solvent (4 mL), 90 ^oC, air, 8 h. [b]Isolated yield.

the yield (compared **3c, f** to **3g, i**). Notably, halogen moieties, such as fluorophenylacetylene, chlorophenylacetylene and bromophenylacetylene were tolerated well with good yield (Scheme 2, **3g-3i**), providing the possibilities for further coupling reaction. Steric hindrance had little effect on this transformation (compared **3b**, **g** to **3j**, **k**). It was found that the heterocyclic derived substrates were also compatible under the optimal conditions (Scheme 2, **3m-3n**). The aliphatic terminal alkyne (hexyne) was also found to be suitable for this reaction but in a low yield (Scheme 2, **3o**). The reaction of various 4-hydroxycoumarin derivatives with phenylacetylene were also summarized in Scheme 2. Both electron-donating groups (4-Me, 3-OMe and 4-OMe) and electron-withdrawing groups (4-F, Cl and Br) could smoothly afford target molecules. Generally, electron-withdrawing groups gave higher yields than those with electron-donating groups (Scheme 2, **3p-3w**).

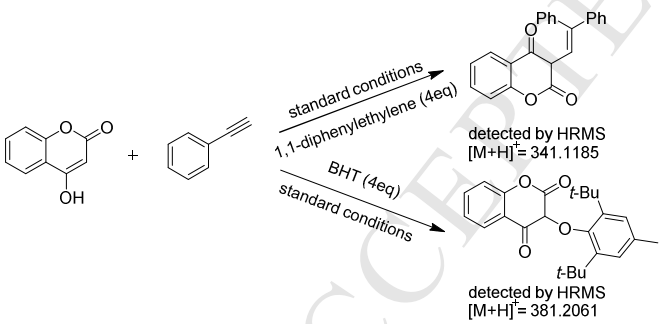
With the scope of the reaction established, some control experiments were carried out. When 4 equiv of 1,1-diphenylethylene or BHT (2,6-di-tert-butyl-4-methylphenol) was added to the reaction system under the standard conditions, no desired compound was obtained and radical addition product was detected by HRMS (Scheme 3). These phenomena indicated that the reaction possibly underwent a radical pathway.

Scheme 2. Scope of terminal alkynes and 4-hydroxycoumarins.[a, b]



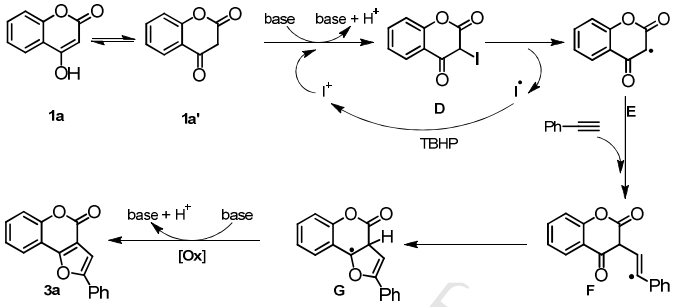
[a]Reaction conditions: 1a (1.5 mmol), 2a (0.5 mmol), I_2 (0.4 mmol), TBHP (1.5 mmol), CH_3COOK (0.5 mmol) and dioxane (4 mL), 90 °C, air, 8 h. [b]Isolated yield.

Scheme 3. Control Experiments for Mechanism



Based on the above results and other literature reports,[11, 12] a possible mechanism is proposed for this transformation in Scheme 4. First, **D** was formed by the oxidation of **1a'** by I^+ which was generated in situ by TBHP and $I^{\cdot}$.[11, 12a] Then **D** generated radical intermidiate **E**. Next, the addition of **E** with alkyne generated vinyl radical intermediate **F**. **F** attacked carbonyl group to give **G**, which was oxidized by TBHP to form target molecule **3a**.

Scheme 4. Proposed mechanism.



3. Conclusions

In summary, we have developed a transition-metal free and simple strategy for the construction of a series of furo[3,2-*c*]coumarins from readily available 4-hydroxycoumarins and terminal alkynes using I_2/TBHP system under a mild air conditions. This method provided an atom-economical, transition-metal free and operationally simple access to the furo[3,2-*c*]coumarins.

4. Experimental section

4.1. General remarks

Substituted substrates **1** were obtained according to the literature reports.[13] Other reagents and solvents were obtained from commercial available and used directly without further purification. All the reactions were monitored by thin-layer chromatography. ^{1}H NMR spectra were recorded on a Bruker Avance 500 spectrometer at 500 MHz using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were run in the same instrument at 125 MHz. HRMS spectra were measured on a Q-TOF instrument in positive-ion mode with an ESI ion source. Melting points were recorded on an XD-4 digital micro melting point apparatus.

4.2. General procedure

4.2.1. Typical Procedure for the Synthesis of 1[13]

In a 250 mL two-neck round-bottom flask, 9 mmol of *o*-hydroxyacetophenone in 15 mL toluene was slowly added to sodium hydride (60% w/w suspension, 5 equiv, 45 mmol, 1.8 g) in toluene (10 mL) under N_2 atmosphere at 0 °C. After 15 min, 13.5 mmol of diethyl carbonate in 10 mL toluene was added dropwise, and the mixture was stirred at room temperature for 30 min and refluxed until the reaction finished (monitored by TLC (Thin Layer Chromatography)). After the mixture cooled to room temperature, the reaction was quenched by slowly addition of 2 N hydrochloric acid. The resulting precipitate was further purified by a short silica gel column chromatography to give a white solid.

*4.2.2. General procedure for preparation of **3** (**3a** as an example)*

A sealed tube was charged with 4-hydroxycoumarin (**1a**) (1.5 mmol, 0.243 g), phenylacetylene (**2a**) (0.5 mmol, 0.051 g), TBHP (1.5 mmol, 0.193 g), I_2 (0.4 mmol, 0.102 g), CH_3COOK (0.5 mmol, 0.049 g) and dioxane (4 mL). Then, the mixture was stirred at 90 °C under air until the reaction was

completed (monitored by TLC). The cooled reaction mixture was diluted with brine and saturated $Na_2S_2O_3$ (20 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layers were dried with Na_2SO_4 and evaporated under vacuum to afford the residue. The residue was purified by column chromatography (silica gel) with petroleum ether/ethyl acetate (50: 1) to obtain pure product **3a** as a yellow solid (77% yield).

4.2.3. 2-Phenyl-4H-furo[3,2-c]chromen-4-one ***(3a)***. Yellow solid (77%), M.P.: 164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (dd, J = 10.0, 1.5 Hz, 1H), 7.82-7.80 (m, 2H), 7.55-7.45 (m, 4H), 7.41-7.36 (m, 2H), 7.18 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.37, 157.02, 156.76, 152.76, 130.76, 129.30, 129.17, 129.10, 124.73, 124.71, 120.94, 117.54, 112.91, 112.66, 102.83; HRMS (ESI) calculated for $C_{17}H_{10}O_3$ $(M+H)^+$ 263.0703; found: 263.0699.

4.2.4. 2-(p-Tolyl)-4H-furo[3,2-c]chromen-4-one ***(3b)***. Yellow solid (77%), M.P.: 176-178 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.91 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.5 Hz, 2H), 7.51-7.48 (m, 1H), 7.43-7.42 (m, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.00-6.94 (m, 3H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.50, 158.44, 156.88, 156.46, 152.56, 130.41, 126.23, 124.62, 121.89, 120.75, 117.43, 114.58, 112.94, 112.71, 101.02, 55.52; HRMS (ESI) calculated for $C_{18}H_{12}O_4$ $(M+H)^+$ 293.0808; found: 293.0794.

4.2.5. 2-(p-Tolyl)-4H-furo[3,2-c]chromen-4-one ***(3c)***. White solid (83%), M.P.: 198-200 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, J = 8.0, 1.5 Hz, 1H), 7.68 (d, J = 8.5 Hz, 2H), 7.52-7.49 (m, 1H), 7.44-7.42 (m, 1H), 7.38-7.34 (m, 1H), 7.26-7.25 (m, 2H), 7.08 (s, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.29, 156.89, 156.58, 152.54, 139.35, 130.44, 129.70, 126.23, 124.54, 124.51, 120.74, 117.35, 112.82, 112.49, 101.88, 21.26; HRMS (ESI) calculated for $C_{18}H_{12}O_3$ $(M+H)^+$ 277.0859; found: 277.0843.

4.2.6. 2-(4-Pentylphenyl)-4H-furo[3,2-c]chromen-4-one ***(3d)***. Yellow solid (79%), M.P.: 156-158 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94-7.92 (m, 1H), 7.72-7.68 (m, 2H), 7.50-7.34 (m, 3H), 7.28-7.26 (m, 2H), 7.09-7.06 (m, 1H), 2.66-2.63 (m, 2H), 1.67-1.63 (m, 2H), 1.38-1.34 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.30, 156.96, 156.60, 152.54, 144.33, 130.44, 129.07, 126.43, 124.56, 124.54, 120.74, 117.35, 112.83, 112.55, 101.86, 35.80, 31.47, 30.98, 22.55, 14.04; HRMS (ESI) calculated for $C_{22}H_{20}O_3$ $(M+H)^+$ 333.1485; found: 333.1488.

4.2.7. 2-(4-Ethoxyphenyl)-4H-furo[3,2-c]chromen-4-one ***(3e)***. Yellow solid (74%), M.P.: 176-178 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (dd, J = 8.0, 1.5 Hz, 1H), 7.71-7.69 (m, 2H), 7.51-7.47 (m, 1H), 7.43-7.42 (m, 1H), 7.37-7.34 (m, 1H), 6.99 (s, 1H), 6.98-6.95 (m, 2H), 4.10 (q, J = 7.0 Hz, 2H), 1.46 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.80, 158.36, 156.86, 156.33, 152.44, 130.28, 126.11, 124.51, 121.61, 120.63, 117.32, 114.96, 112.85, 112.61, 100.82, 63.66, 14.78; HRMS (ESI) calculated for $C_{19}H_{14}O_4$ $(M+H)^+$ 307.0965; found: 307.0970.

4.2.8. 2-(4-Ethylphenyl)-4H-furo[3,2-c]chromen-4-one ***(3f)***. White solid (88%), M.P.: 148-150 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93-7.91 (m, 1H), 7.70-7.68 (m, 2H), 7.51-7.48 (m, 1H), 7.43-7.41 (m, 1H), 7.37-7.34 (m, 1H), 7.29-7.27 (m, 2H), 7.09-7.08 (m, 1H), 2.71 (q, J = 7.5 Hz, 2H), 1.29 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.31, 156.91, 156.59, 152.51, 145.67, 130.44, 128.52, 126.43, 124.60, 124.54, 120.74, 117.33, 112.80, 112.52, 101.89, 28.76, 15.39; HRMS (ESI) calculated for $C_{19}H_{14}O_3$ $(M+H)^+$ 291.1016; found: 291.1002.

4.2.9. 2-(4-Fluorophenyl)-4H-furo[3,2-c]chromen-4-one ***(3g)***. Yellow solid (45%), M.P.: 216-218 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.95 (dd, J = 8.0, 1.0 Hz, 1H), 7.81-7.79 (m, 2H), 7.55-7.52 (m, 1H), 7.47-7.45 (m, 1H), 7.40-7.37 (m, 1H), 7.19-7.16 (m, 2H), 7.12 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.16 (d, J = 248.8 Hz), 158.16, 156.90, 155.73, 152.64, 130.71, 126.58 (d, J = 7.5 Hz), 125.35 (d, J = 2.5 Hz), 124.64, 120.76, 117.45, 116.35 (d, J = 22.5 Hz), 112.70, 112.55, 102.43; HRMS (ESI) calculated for $C_{17}H_9FO_3$ $(M+H)^+$ 281.0608; found: 281.0608.

4.2.10. 2-(4-Bromophenyl)-4H-furo[3,2-c]chromen-4-one ***(3h)***. White solid (30%), M.P.: 260-262 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (dd, J = 7.5, 1.5 Hz, 1H), 7.69-7.68 (m, 2H), 7.62-7.61 (m, 2H), 7.57-7.53 (m, 1H), 7.48-7.46 (m, 1H), 7.41-7.38 (m, 1H), 7.20 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 150.09, 157.09, 155.51, 152.71, 135.08, 130.85, 129.35, 127.47, 125.81, 124.67, 120.84, 117.49, 112.65, 112.55, 103.20; HRMS (ESI) calculated for $C_{17}H_9BrO_3$ $(M+H)^+$ 340.9808; found: 340.9816.

4.2.11. 2-(4-Chlorophenyl)-4H-furo[3,2-c]chromen-4-one ***(3i)***. White solid (32%), M.P.: 270-272 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97-7.95 (m, 1H), 7.76-7.74 (m, 2H), 7.57-7.53 (m, 1H), 7.48-7.45 (m, 3H), 7.41-7.38 (m, 1H), 7.18 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.09, 157.09, 155.51, 152.71, 135.08, 130.85, 129.35, 127.47, 125.81, 124.67, 120.84, 117.49, 112.65, 112.55, 103.20; HRMS (ESI) calculated for $C_{17}H_9ClO_3$ $(M+H)^+$ 297.0313; found: 297.0300.

4.2.12. 2-(3-Methoxyphenyl)-4H-furo[3,2-c]chromen-4-one ***(3j)***. White solid (81%), M.P.: 180-182 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (dd, J = 7.5, 1.5 Hz, 1H), 7.54-7.51 (m, 1H), 7.45-7.44 (m, 1H), 7.39-7.36 (m, 3H), 7.320-7.317 (m, 1H), 7.16 (s, 1H), 6.94-6.92 (m, 1H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.04, 158.20, 156.86, 156.41, 152.63, 130.65, 130.17, 130.16, 124.59, 120.83, 117.39, 117.11, 114.65, 112.73, 112.48, 110.14, 103.01, 55.42; HRMS (ESI) calculated for $C_{18}H_{12}O_4$ $(M+H)^+$ 293.0808; found: 293.0813.

4.2.13. 2-(2-Fluorophenyl)-4H-furo[3,2-c]chromen-4-one ***(3k)***. White solid (48%), M.P.: 158-460 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93-7.89 (m, 2H), 7.52-7.49 (m, 1H), 7.41-7.39 (m, 1H), 7.37-7.31 (m, 3H), 7.25-7.24 (m, 1H), 7.17-7.13 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.08 (d, J = 251.4 Hz), 158.00, 156.47, 152.67, 150.58 (d, J = 3.1 Hz), 130.83, 130.26 (d, J = 8.5 Hz), 126.25, 124.60, 124.57 (d, J = 3.5 Hz), 120.85, 117.36, 117.26, 116.37 (d, J = 21.1 Hz), 112.59, 112.47, 107.67 (d, J = 12.9 Hz); HRMS (ESI) calculated for $C_{17}H_9FO_3$ $(M+H)^+$ 281.0608; found: 281.0615.

4.2.14. 2-(3-Fluorophenyl)-4H-furo[3,2-c]chromen-4-one ***(3l)***. Yellow solid (64%), M.P.: 176-178 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, J = 8.0, 1.5 Hz, 1H), 7.56-7.51 (m, 2H), 7.49-7.36 (m, 4H), 7.17 (s, 1H), 7.09-7.06 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 164.11 (d, J = 245.3 Hz), 157.97, 157.11, 155.19

(d, *J* = 3.0 Hz), 152.71, 130.93, 130.85, 130.81 (d, *J* = 8.4 Hz), 124.69, 120.86, 120.25 (d, *J* = 3.0 Hz), 117.44, 116.10 (d, *J* = 21.3 Hz), 112.53, 112.44, 111.56 (d, *J* = 23.8 Hz), 103.76; HRMS (ESI) calculated for $C_{17}H_9FO_3$ $(M+H)^+$ 281.0608; found: 281.0627.

4.2.15. 2-(Thiophen-2-yl)-4H-furo[3,2-c]chromen-4-one ***(3m)***. Yellow solid (49%), M.P.: 160-162 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.91 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.52-7.48 (m, 1H), 7.46-7.45 (m, 1H), 7.43-7.41 (m, 1H), 7.38-7.33 (m, 2H), 7.12-7.10 (m, 1H), 6.98 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 157.96, 156.41, 152.57, 151.92, 131.38, 130.63, 128.07, 126.52, 125.12, 124.60, 120.80, 117.33, 112.55, 112.48, 102.35; HRMS (ESI) calculated for $C_{15}H_8O_3S$ $(M+H)^+$ 269.0267; found: 269.0276.

4.2.16. 2-(Thiophen-3-yl)-4H-furo[3,2-c]chromen-4-one ***(3n)***. Yellow solid (61%), M.P.: 142-144 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.86-7.85 (m, 1H), 7.671-7.665 (m, 1H), 7.49-7.46 (m, 1H), 7.40-7.31 (m, 4H), 6.93-6.92 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 158.10, 156.32, 153.32, 152.52, 130.51, 130.50, 127.12, 124.67, 124.53, 121.74, 120.68, 117.29, 112.63, 112.27, 102.21; HRMS (ESI) calculated for $C_{15}H_8O_3S$ $(M+H)^+$ 269.0267; found: 269.0275.

4.2.17. 2-Butyl-4H-furo[3,2-c]chromen-4-one ***(3o)***. Yellow liquid (17%); ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.85 (d, *J* = 7.5 Hz, 1H), 7.50-7.42 (m, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 6.58 (s, 1H), 2.82 (t, *J* = 7.5 Hz, 2H), 1.77 (quint, *J* = 7.5 Hz, 2H), 1.48 (sext, *J* = 7.5 Hz, 2H), 0.99 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 160.12, 158.50, 156.56, 152.35, 130.09, 124.37, 120.59, 117.28, 113.03, 111.50, 103.35, 29.74, 27.78, 22.15, 13.72; HRMS (ESI) calculated for $C_{15}H_{14}O_3$ $(M+H)^+$ 243.1016; found: 243.1005.

4.2.18. 8-Methoxy-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3p)***. Yellow solid (60%), M.P.: 162-164 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.78-7.76 (m, 2H), 7.47-7.44 (m, 2H), 7.39-7.36 (m, 1H), 7.33 (d, *J* = 9.5 Hz, 1H), 7.28-7.27 (m, 1H), 7.11 (s, 1H), 7.06 (dd, *J* = 9.0, 4.0 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 158.28, 156.69, 156.55, 156.33, 147.09, 129.14, 129.00, 128.91, 124.54, 118.55, 118.51, 112.92, 112.67, 102.77, 55.95; HRMS (ESI) calculated for $C_{18}H_{12}O_4$ $(M+H)^+$ 293.0808; found: 293.0806.

4.2.19. 7-Methoxy-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3q)***. Yellow solid (61%), M.P.: 198-200 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.84 (d, *J* = 8.5 Hz, 1H), 7.79-7.77 (m, 2H), 7.48-7.44 (m, 2H), 7.39-7.36 (m, 1H), 7.12 (s, 1H), 6.96-6.94 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 162.00, 158.56, 157.60, 155.71, 154.41, 129.13, 128.99, 128.88, 124.39, 121.78, 112.89, 110.03, 106.18, 102.50, 101.49, 56.06; HRMS (ESI) calculated for $C_{18}H_{12}O_4$ $(M+H)^+$ 293.0808; found: 293.0821.

4.2.20. 8-Methyl-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3r)***. Yellow solid (66%), M.P.: 148-150 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.79-7.73 (m, 2H), 7.69 (s, 1H), 7.47-7.44 (m, 2H), 7.39-7.36 (m, 1H), 7.32-7.28 (m, 2H), 7.13 (s, 1H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 158.38, 156.89, 156.41, 150.84, 134.44, 131.66, 129.07, 129.00, 124.51, 120.48, 117.08, 112.40, 112.39, 102.67, 20.96; HRMS (ESI) calculated for $C_{18}H_{12}O_3$ $(M+H)^+$ 277.0859; found: 277.0849.

4.2.21. 2-(4-Methoxyphenyl)-8-methyl-4H-furo[3,2-c]chromen-4-one ***(3s)***. Yellow solid (75%), M.P.: 184-186 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.69-7.64 (m, 3H), 7.29-7.25 (m, 2H), 6.96-6.94 (m, 3H), 3.85 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 160.33, 158.47, 156.55, 156.35, 150.64, 134.33, 131.33, 126.03, 121.83, 120.31, 116.98, 114.43, 112.47, 112.44, 100.88, 55.39, 20.95; HRMS (ESI) calculated for $C_{19}H_{14}O_4$ $(M+H)^+$ 307.0965; found: 307.0964.

4.2.22. 8-Fluoro-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3t)***. Yellow solid (74%), M.P.: 218-220 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.81-7.80 (m, 2H), 7.63-7.60 (m, 1H), 7.50-7.47 (m, 2H), 7.44-7.40 (m, 2H), 7.25-7.21 (m, 1H), 7.18 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 160.00 (d, *J* = 243.6 Hz), 157.80, 157.24, 155.95 (d, *J* = 2.9 Hz), 148.70, 129.43, 129.10, 128.75, 124.68, 119.15 (d, *J* = 8.5 Hz), 118.08 (d, *J* = 24.5 Hz), 113.53 (d, *J* = 9.6 Hz), 113.25, 106.75 (d, *J* = 25.8 Hz), 102.78; HRMS (ESI) calculated for $C_{17}H_9FO_3$ $(M+H)^+$ 281.0608; found: 281.0620.

4.2.23. 7-Fluoro-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3u)***. White solid (72%), M.P.: 176-178 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.92-7.90 (m, 1H), 7.77-7.75 (m, 2H), 7.47-7.44 (m, 2H), 7.40-7.37 (m, 1H), 7.16-7.10 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 164.73 (d, *J* = 251.3 Hz), 157.80, 156.57, 156.44, 153.66 (d, *J* = 13.75 Hz), 129.23, 129.05, 128.77, 124.51, 122.31 (d, *J* = 10.0 Hz), 112.86 (d, *J* = 22.5 Hz), 111.42, 109.52 (d, *J* = 2.5 Hz), 105.22 (d, *J* = 25.0 Hz), 102.50; HRMS (ESI) calculated for $C_{17}H_9FO_3$ $(M+H)^+$ 281.0608; found: 281.0605.

4.2.24. 8-Chloro-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3v)***. Yellow solid (85%), M.P.: 212-214 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.92 (d, *J* = 2.5 Hz, 1H), 7.82-7.80 (m, 2H), 7.50-7.45 (m, 3H), 7.43-7.38 (m, 2H), 7.18 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 157.60, 157.31, 155.50, 150.88, 130.52, 130.19, 129.46, 129.11, 128.67, 124.68, 120.32, 118.84, 113.80, 113.26, 102.76; HRMS (ESI) calculated for $C_{17}H_9ClO_3$ $(M+H)^+$ 297.0313; found: 297.0325.

4.2.25. 8-Bromo-2-phenyl-4H-furo[3,2-c]chromen-4-one ***(3w)***. White solid (61%), M.P.: 204-206 °C; ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 8.053-8.049 (m, 1H), 7.80-7.79 (m, 2H), 7.60 (dd, *J* = 9.0, 2.5 Hz, 1H), 7.49-7.46 (m, 2H), 7.42-7.39 (m, 1H), 7.33 (d, *J* = 8.5 Hz, 1H), 7.16 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): *δ* 157.51, 157.30, 155.31, 151.33, 133.39, 129.46, 129.10, 128.63, 124.67, 123.30, 119.10, 117.47, 114.25, 113.25, 102.74; HRMS (ESI) calculated for $C_{17}H_9BrO_3$ $(M+H)^+$ 340.9808; found: 340.9817.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at t http:// dx.doi.org/

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