



Cite this: *RSC Adv.*, 2019, 9, 32946

# Oxidant-free, three-component synthesis of 7-amino-6*H*-benzo[*c*]chromen-6-ones under green conditions†

B. S. Vachan,<sup>a</sup> Aishwarya Ramesh,<sup>a</sup> Muthu Karuppasamy,<sup>a</sup> Isravel Muthukrishnan,<sup>a</sup> Subbiah Nagarajan,<sup>b</sup> J. Carlos Menéndez,<sup>c</sup> C. Uma Maheswari<sup>\*a</sup> and Vellaisamy Sridharan<sup>†ad</sup>

An oxidant-free three-component synthesis of biologically significant 7-amino-6*H*-benzo[*c*]chromen-6-ones was established involving a Sc(OTf)<sub>3</sub> catalyzed three-component reaction between primary amines, β-ketoesters and 2-hydroxychalcones under green conditions. In this strategy, both the B and C rings of 6*H*-benzo[*c*]chromen-6-ones were constructed simultaneously starting from acyclic precursors by generating four new bonds including two C–C, one C–N and one C–O in a single synthetic operation. The mechanism of this sequential cascade process involves the initial formation of a β-enaminone intermediate followed by Michael addition with 2-hydroxychalcone, intramolecular cyclization, dehydration, lactonization and aromatization steps. Unlike the related literature approaches, this reaction delivered the products without the addition of any external oxidants to achieve the key aromatization step.

Received 5th September 2019

Accepted 3rd October 2019

DOI: 10.1039/c9ra07108c

rsc.li/rsc-advances

## Introduction

Among the many biologically valuable oxygen heterocycles, 6*H*-benzo[*c*]chromen-6-ones, which belong to an important group of heptaketide coumarin derivatives, are the core structure of a variety of biologically significant natural and synthetic compounds.<sup>1</sup> These secondary metabolites, represented by graphis lactone A **1**,<sup>2</sup> alternariol **2**,<sup>3</sup> defucogivocarcin V **3**,<sup>4</sup> and palmariol A and B (**4** and **5**)<sup>5</sup> have predominantly been isolated from fungi, lichens, bacteria, plants, and animal waste, and are known to exhibit numerous potential biological activities including acting as an antioxidant *via* free radical scavenging, and antiviral, antimicrobial, cytotoxic, antineoplastic and acetylcholinesterase inhibitory activities (Fig. 1). Other significant activities of 6*H*-benzo[*c*]chromen-6-one derivatives include anti-inflammatory, estrogenic activity, DNA gyrase inhibitory

activity, casein kinase 2 (CK2) inhibitory activity, DNA intercalative activity, and many others.<sup>1,6</sup>

Owing to the biological significance of 6*H*-benzo[*c*]chromen-6-ones, the synthesis of derivatives of this framework remain an attractive goal for synthetic chemists.<sup>7</sup> Surprisingly, however, most of the existing approaches for the synthesis of 6*H*-benzo[*c*]chromen-6-ones involve the construction of the B ring (lactone ring) from biphenyl derivatives *via* lactonization reactions, CO insertion *etc.* Alternatively, the B ring was generated from two different aryl derivatives by simultaneous formation of the C–C

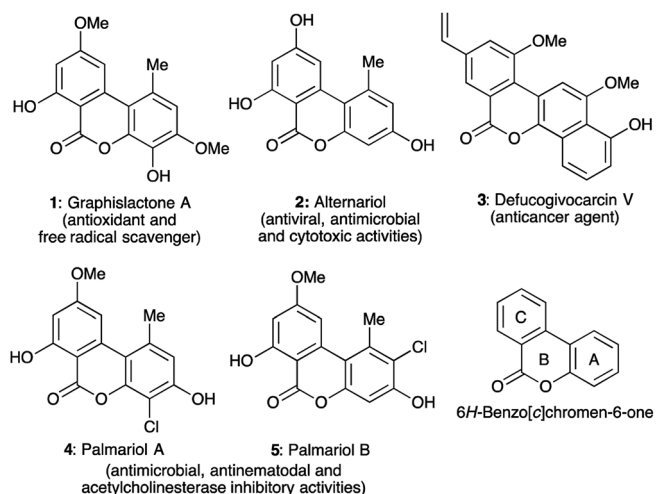


Fig. 1 Selected biologically important natural 6*H*-benzo[*c*]chromen-6-ones.

<sup>a</sup>Department of Chemistry, School of Chemical and Biotechnology, SASTRA Deemed University, Thanjavur-613401, Tamil Nadu, India. E-mail: umamaheswari@sast. sastra.edu; uma.cchem@gmail.com

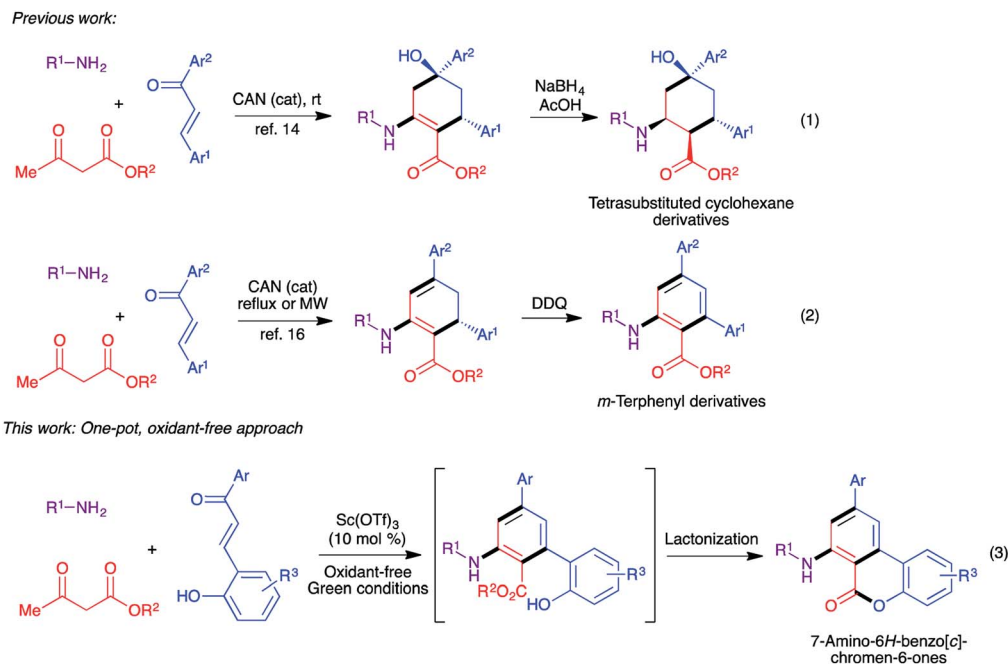
<sup>b</sup>Department of Chemistry, National Institute of Technology, Warangal, Warangal-506004, Telangana, India

<sup>c</sup>Unidad de Química Orgánica y Farmacéutica, Departamento de Química en Ciencias Farmacéuticas, Facultad de Farmacia, Universidad Complutense, 28040 Madrid, Spain

<sup>d</sup>Department of Chemistry and Chemical Sciences, Central University of Jammu, Rahya-Suchani (Bagla), District-Samba, Jammu-181143, J&K, India. E-mail: vesridharan@gmail.com; sridharan.che@ujammu.ac.in

† Electronic supplementary information (ESI) available: <sup>1</sup>H and <sup>13</sup>C NMR spectra of new products. See DOI: 10.1039/c9ra07108c





Scheme 1 Previous annulation reactions and the hypothesis of the present work.

bond between the A and C rings and lactonization reactions.<sup>8</sup> The green protocol developed by Song and Chi involving a base mediated reaction between unsaturated aldehydes and coumarins, through a formal [4+2] process,<sup>9</sup> and Bodwell's inverse electron demand Diels–Alder reaction strategy<sup>10</sup> are significant approaches among the very few existing methods comprising the generation of the C ring. In addition, Fan and co-workers established the synthesis of aminonaphthochromenones starting from 2-[(2-hydroxyphenyl)ethynyl]benzonitriles and Reformatsky reagents by constructing both B and C rings.<sup>11</sup> Poudel and Lee have also developed a base-promoted two-component reaction between 2-hydroxychalcones and  $\beta$ -ketoesters for the synthesis of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones in moderate yields.<sup>12</sup> Almost simultaneously, five examples of 7-hydroxy-6*H*-benzo[*c*]chromen-6-ones were synthesized using a diethylamine-catalyzed approach in 51–59% yield.<sup>13</sup> Despite these few methods, the synthesis of 6*H*-benzo[*c*]chromen-6-ones from readily available starting materials *via* multicomponent reactions remains almost unexplored. Consequently, we envisioned to develop a straightforward, oxidant-free, three-component, one-pot approach for the synthesis of 7-amino-6*H*-benzo[*c*]chromen-6-ones involving the simultaneous generation of both the B and C rings.

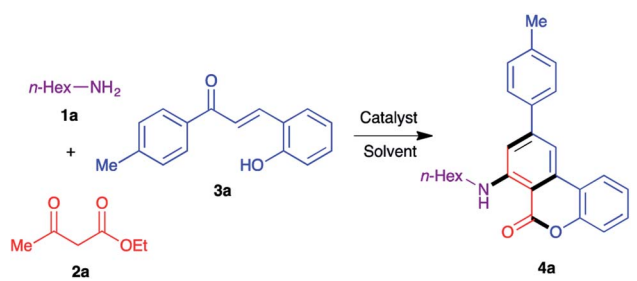
## Results and discussion

A decade ago we established a diastereoselective two-step synthesis of densely functionalized cyclohexane derivatives involving a cerium(iv) ammonium nitrate (CAN)-catalyzed three-component reaction between alkylamines,  $\beta$ -ketoesters, and chalcones (Scheme 1, eqn (1)).<sup>14,15</sup> The key step in this reaction involves the formation of a  $\beta$ -enaminoester from alkylamines and  $\beta$ -ketoesters followed by a Michael addition to the chalcone

component and an intramolecular cyclization to generate the cyclohexene ring from the acyclic precursors. Subsequently, we extended this approach to the synthesis of *m*-terphenyl derivatives by slightly modifying the reaction conditions (Scheme 1, eqn (2)).<sup>16</sup> However, the final aromatization step required the use of one equivalent of DDQ. Yaragorla and Dada have also demonstrated a similar strategy for the synthesis of the related compounds, including 6*H*-benzo[*c*]chromen-6-ones, using  $\text{Ca}(\text{OTf})_2/n\text{-Bu}_4\text{NPF}_6$  as catalyst and one equivalent of chloranil as oxidant.<sup>17</sup> With these precedents, we herein describe a domino process that combines the three-component synthesis of cyclohexene derivatives and aromatization-lactonization steps for the synthesis of 7-amino-6*H*-benzo[*c*]chromen-6-ones starting from primary amines,  $\beta$ -ketoesters, and 2-hydroxychalcones in one-pot under oxidant-free green conditions by generating both B and C rings simultaneously (Scheme 1, eqn (3)).

We began our optimization studies by using *n*-hexylamine **1a**, ethyl acetoacetate **2a** and (*E*)-3-(2-hydroxyphenyl)-1-(*p*-tolyl) prop-2-en-1-one **3a** as model substrates to identify the suitable reaction conditions for the proposed three-component reaction. At the outset, we employed the previously established reaction conditions (10 mol% of CAN, ethanol, 80 °C) and 30% of the product **4a** was isolated after 30 h (Table 1, entry 1). When the catalyst load was increased to 20 mol%, no significant improvement was observed (38%, entry 1). In order to increase the product yield we performed the reaction in *t*-BuOH and some green solvents such as PEG-200 and glycerol, but only 19–42% yield was observed (entries 2–4). Use of *t*-butyl acetoacetate as the starting material instead of ethyl acetoacetate failed to improve the yield significantly (39%, entry 5). We then tested other Lewis acids such as  $\text{InCl}_3$ ,  $\text{BiCl}_3$ ,  $\text{BF}_3 \cdot \text{OEt}_2$ ,  $\text{AgOTf}$  and  $\text{Yb}(\text{OTf})_3$  in ethanol at 90 °C (entries 6–10). Encouragingly,



Table 1 Optimization of reaction conditions<sup>a</sup>


Entry	Catalyst	Solvent	Temp. (°C)	Time (h)	Yield of 4a <sup>b</sup> (%)
1	CAN	EtOH	80	30	30 (38) <sup>f</sup>
2	CAN	<i>t</i> -BuOH	80	30	42
3	CAN	PEG-200	80	30	22
4	CAN	Glycerol	80	30	19
5 <sup>d</sup>	CAN	EtOH	90	30	39
6	InCl <sub>3</sub>	EtOH	90	24	42
7	BiCl <sub>3</sub>	EtOH	90	24	21
8	BF <sub>3</sub> ·OEt <sub>2</sub>	EtOH	90	24	14
9	AgOTf	EtOH	90	20	59
10	Yb(OTf) <sub>3</sub>	EtOH	90	24	65
11	Sc(OTf) <sub>3</sub>	EtOH	90	20	73
12 <sup>e</sup>	Sc(OTf) <sub>3</sub>	EtOH	90	20	78
13 <sup>e</sup>	Sc(OTf) <sub>3</sub>	MeOH	70	20	67
14 <sup>e</sup>	Sc(OTf) <sub>3</sub>	<i>i</i> -PrOH	100	20	59
15 <sup>e</sup>	Sc(OTf) <sub>3</sub>	<i>t</i> -BuOH	100	20	58
16	Sc(OTf) <sub>3</sub>	PEG-200	100	20	49
17 <sup>f,g</sup>	Sc(OTf) <sub>3</sub>	Glycerol	100	24	76 (72) <sup>d,h</sup>
18	Sc(OTf) <sub>3</sub>	Water	100	20	42
19	—	Glycerol	100	30	Traces <sup>i</sup>

<sup>a</sup> Unless otherwise noted, all reactions were carried out with **1a** (0.6 mmol), **2a** (0.5 mmol) and **3a** (0.5 mmol) with 10 mol% catalyst in 3 mL solvent.

<sup>b</sup> Isolated yield. <sup>c</sup> 20 mol% of catalyst was used. <sup>d</sup> *t*-Butyl acetoacetate was used instead of ethyl acetoacetate. <sup>e</sup> 1.5 mL of solvent was used.

<sup>f</sup> The reaction did not proceed at room temperature. <sup>g</sup> Optimized reaction conditions. <sup>h</sup> Under nitrogen atmosphere 22% of the product was obtained. <sup>i</sup> Formation of intermediate  $\beta$ -enaminoester was observed.

AgOTf and Yb(OTf)<sub>3</sub> afforded the product **4a** in 59% and 65% yields respectively (entries 9 and 10). Next, Sc(OTf)<sub>3</sub> was tested as catalyst and the reaction delivered 73% of the product **4a** in 20 h (entry 11). Interestingly, when concentration was increased (1.5 mL of solvent at 0.5 mmol scale), the yield was increased to 78% (entry 12). Further attempts to improve the product yield by using other protic solvents including MeOH, *i*-PrOH and *t*-BuOH were not successful (entries 13–15). Finally, in order to achieve a green protocol for this three-component cascade process, the reaction was carried out in a set of common green solvents such as PEG-200, glycerol and water in the presence of Sc(OTf)<sub>3</sub> (entries 16–18). Among the tested solvents, glycerol delivered a comparable yield to ethanol at 100 °C in the absence of any oxidant in 24 h (76%, entry 17) and the other two green solvents gave moderate yields of 42–49%. To understand the role of the catalyst in this transformation, we performed the reaction in the absence of any catalyst in glycerol at 100 °C, where only the intermediate  $\beta$ -enaminoester obtained from the amine and ethyl acetoacetate was observed in the crude reaction

mixture (entry 19). The crucial role of oxygen (air) in this transformation was also demonstrated by performing the reaction under nitrogen atmosphere where only 22% of the product was isolated together with some unidentified mixture (entry 17). In conclusion, the use of 10 mol% of Sc(OTf)<sub>3</sub> as catalyst in glycerol at 100 °C was selected as the optimized reaction condition for further experiments.

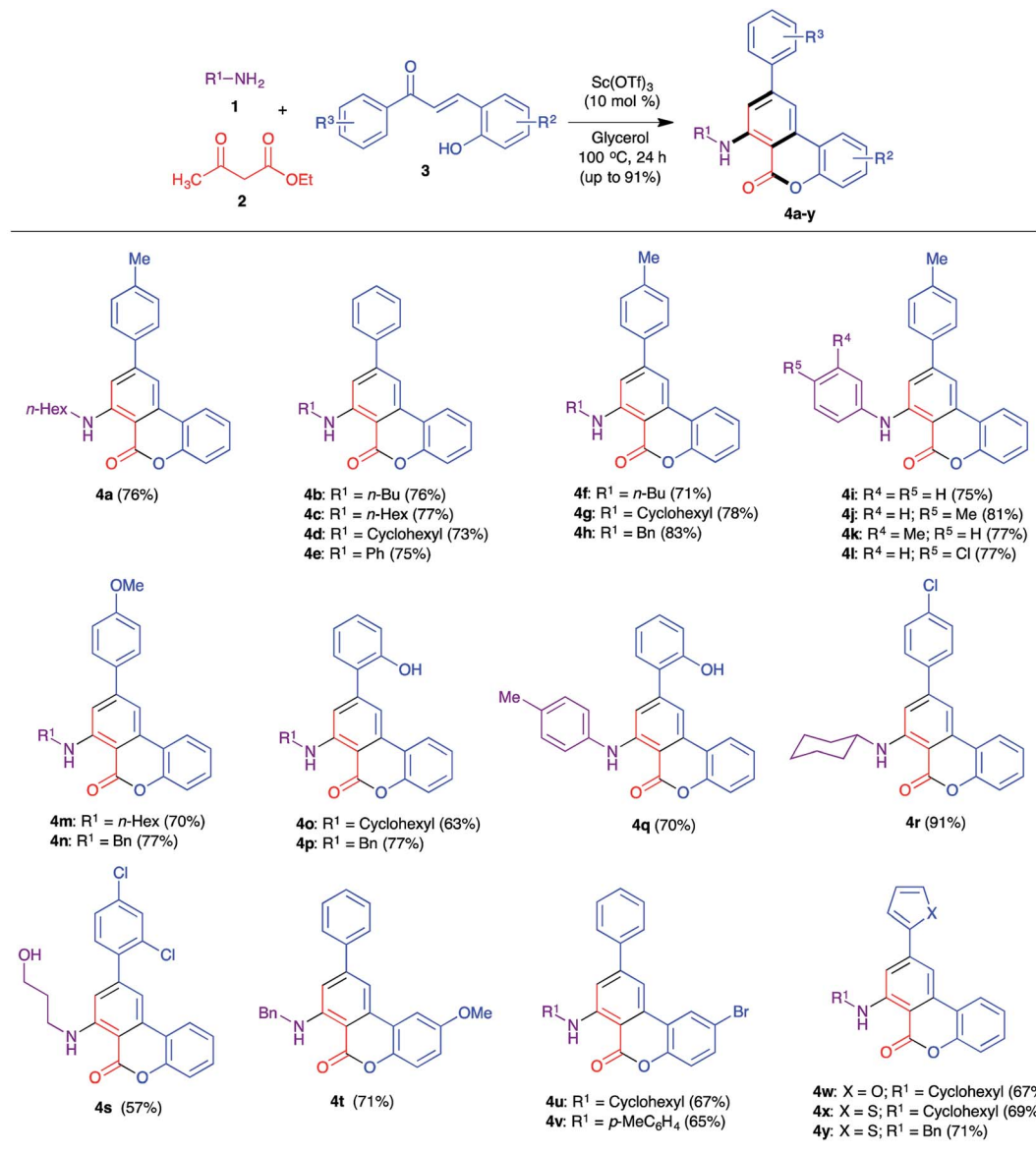
After having optimized the reaction conditions, we turned to explore the scope and limitations of the three-component reaction by employing a variety of primary amines,  $\beta$ -ketoesters and 2-hydroxychalcones bearing a large number of substituents on both the aryl rings (Scheme 2). At the outset, the effect of the primary amines, including alkyl and arylamines, was investigated. The combination of ethyl acetoacetate, unsubstituted 2-hydroxychalcones and alkyl amines including *n*-butylamine, *n*-hexylamine, cyclohexylamine and aniline delivered the corresponding 6*H*-benzo[*c*]chromen-6-ones **4b–4e** in good yields (73–77%). Likewise, *n*-butylamine, cyclohexylamine and benzylamine were also reacted with chalcone **3a** to furnish the products **4f–4h** in 71–83% yields. Arylamines including aniline and its *p*-Me, *m*-Me and *p*-Cl derivatives also reacted smoothly under the optimized conditions to afford the corresponding diarylamine derivatives **4i–4l** in comparable yields (75–81%). Subsequently, we varied the substituents in the 2-hydroxychalcone component, where substituents including 4'-OMe (**4m**, **4n**), 2'-OH (**4o–4q**) and 4'-Cl (**4r**) were well tolerated, and delivered the products in good yields (63–91%). A maximum yield of 91% was observed for the combination of cyclohexylamine and the 4'-Cl substituted chalcone (**4r**). 3-Aminopropanol and 2',4'-dichlorochalcone were also reacted with ethyl acetoacetate and furnished the product **4s** in 57% yield. Both electron-donating (OMe, **4t**) and withdrawing (Br, **4u** and **4v**) substituents were introduced in the 2-hydroxy aryl ring and these chalcones also reacted well to give the respective 6*H*-benzo[*c*]chromen-6-ones in 65–71% yields. Finally, chalcones bearing heteroaryl rings such as 2-furyl and 2-thienyl were also tested and 67–71% yields of products (**4w–4y**) were obtained.

A mechanism is proposed involving the formation of  $\beta$ -enaminoester **A**, starting from primary amines **1** and ethyl acetoacetate **2**, based on our previous reports<sup>14,16</sup> (Scheme 3). The *in situ* generated  $\beta$ -enaminoester **A**, in the presence of the Lewis acid catalyst,<sup>18,19</sup> undergoes a Michael addition with 2-hydroxychalcone **3** followed by intramolecular cyclization and dehydration to deliver the cyclohexene derivative **B**. Final lactonization and aromatization reactions under the experimental conditions, in the absence of an oxidant different from air, furnished the final products **4**.

## Conclusions

In conclusion, we have demonstrated a simple three-component protocol for the synthesis of biologically relevant 7-amino-6*H*-benzo[*c*]chromen-6-ones under green conditions. The Sc(OTf)<sub>3</sub> catalyzed three-component reaction between primary amines,  $\beta$ -ketoesters and 2-hydroxychalcones afforded the title compounds in good yields by generating four new bonds including two C–C, one C–N and one C–O bonds, and two rings (one carbo- and one heterocycle) in a single synthetic





Scheme 2 Substrate scope for the three-component synthesis of 6H-benzol[c]chromen-6-ones.

operation. The reaction was found to be general and a variety of substituents were tolerated on both the primary amines and 2-hydroxychalcones. The mechanism of this cascade reaction involves the initial reaction between primary amines and  $\beta$ -ketoesters in the presence of Sc(OTf)<sub>3</sub> to deliver the  $\beta$ -enamine intermediate followed by Michael addition with  $\alpha,\beta$ -unsaturated ketones to furnish the products *via* intramolecular cyclization, dehydration, lactonization and aromatization steps in one-pot. Notably, the reaction delivered the products with no external oxidants to achieve the key aromatization reaction unlike the related reports available in literature.

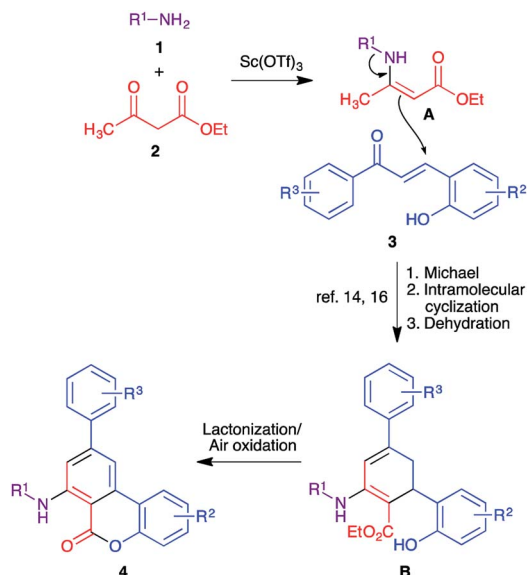
## Experimental section

### General information

All reagents and solvents were purchased from commercial suppliers (Avra, Alfa Aesar, Sigma-Aldrich, CDH, Merck) and

used without further purification. All reactions were carried out in oven-dried glassware under air atmosphere. The reactions were monitored by thin layer chromatography using Merck silica gel 60 F<sub>254</sub> and visualized by UV detection or using *p*-anisaldehyde stain or molecular iodine. Silica gel (230–400 mesh) was used for flash column chromatography. Melting points were recorded on a melting point apparatus in capillaries and are uncorrected. <sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded in CDCl<sub>3</sub> or DMSO-d<sub>6</sub> at room temperature on a Bruker Avance 300 spectrometer operating at 300 MHz for <sup>1</sup>H and 75 MHz for <sup>13</sup>C. Chemical shifts ( $\delta$ ) are expressed in ppm using TMS as an internal standard and coupling constants (*J*) are given in Hz. Infrared (IR) spectra were obtained using an Agilent Cary630 FTIR Spectrometer with a diamond ATR accessory for solid and liquid samples, requiring no sample preparation and the major frequencies were reported in cm<sup>-1</sup>. Elemental analyses were determined at the CAI de Microanálisis Elemental, Universidad





Scheme 3 Proposed mechanism for the three-component synthesis of 6H-benzo[c]chromen-6-ones.

Complutense, by using a Leco 932 CHNS combustion microanalyzer.

### General procedure for the synthesis of 6H-benzo[c]chromen-6-ones 4a–y

To a stirred solution of primary amine **1** (1.2 mmol, 1.2 equiv.) in glycerol (6 mL) was added  $\beta$ -ketoester **2** (1.0 mmol, 1.0 equiv.) and  $\text{Sc}(\text{OTf})_3$  (10 mol%). The reaction mixture was stirred at room temperature for 15 minutes and then chalcone **3** (1.0 mmol, 1.0 equiv.) was added, and the reaction mixture was stirred at 100 °C for 24 h. After completion of the reaction, the mixture was diluted with ethyl acetate (20 mL) and washed with water followed by brine. The solvent was evaporated under reduced pressure and the crude product was purified through silica column chromatography using petroleum ether-ethyl acetate mixture (96 : 4 to 90 : 10, v/v) as eluent to obtain compounds **4**.

**7-(Hexylamino)-9-(*p*-tolyl)-6H-benzo[c]chromen-6-one (4a).** Yellow solid; mp: 114–116 °C; yield: 0.293 g, 76%; IR (neat): 3333.5, 3025.4, 2951.4, 2924.8, 2862.6, 1679.1, 1559.7, 1446.0, 1383.5, 1249.3, 1207.3, 1091.6  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  0.84 (t,  $J = 6.9$  Hz, 3H), 1.28 (sextet,  $J = 3.3$  Hz, 4H), 1.41 (quin,  $J = 7.5$  Hz, 2H), 1.71 (quin,  $J = 6.9$  Hz, 2H), 2.37 (s, 3H), 3.24 (t,  $J = 7.2$  Hz, 2H), 6.83 (d,  $J = 0.9$  Hz, 1H), 7.21–7.25 (m, 4H), 7.34–7.38 (m, 2H), 7.52 (d,  $J = 8.1$  Hz, 2H), 7.99 (dd,  $J = 6.9, 1.2$  Hz, 1H), 8.65 (brs, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1, 21.3, 22.6, 26.9, 28.9, 31.6, 43.2, 101.6, 106.3, 108.1, 117.3, 118.9, 123.2, 124.1, 127.3, 129.6, 129.9, 136.4, 137.9, 138.5, 148.5, 151.2, 152.5, 163.3; anal. calcd for  $\text{C}_{26}\text{H}_{27}\text{NO}_2$ : C, 81.01; H, 7.06; N, 3.63. Found: C, 80.82; H, 7.01; N, 3.55.

**7-(Butylamino)-9-phenyl-6H-benzo[c]chromen-6-one (4b).** Yellow solid; mp: 190–192 °C (Lit. 193–194 °C);<sup>17</sup> yield: 0.261 g, 76%; IR (neat): 3322.5, 3059.3, 2952.1, 2927.2, 2864.3, 1676.3, 1609.0, 1561.7, 1447.2, 1376.1, 1245.8, 1205.6  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR

(300 MHz,  $\text{CDCl}_3$ ):  $\delta$  0.93 (t,  $J = 7.2$  Hz, 3H), 1.45 (sextet,  $J = 7.2$  Hz, 2H), 1.70 (quin,  $J = 7.2$  Hz, 2H), 3.26 (q,  $J = 6.9$  Hz, 2H), 6.79 (d,  $J = 1.2$  Hz, 1H), 7.21–7.25 (m, 2H), 7.34–7.47 (m, 5H), 7.62 (td,  $J = 6.6, 1.5$  Hz, 2H), 8.00 (dd,  $J = 7.8, 1.2$  Hz, 1H), 8.53 (t,  $J = 4.5$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.9, 20.4, 31.0, 42.9, 101.8, 106.5, 108.4, 117.3, 118.9, 123.3, 124.2, 127.4, 128.5, 128.9, 130.0, 136.5, 140.9, 148.6, 151.1, 152.5, 163.3; anal. calcd for  $\text{C}_{23}\text{H}_{21}\text{NO}_2$ : C, 80.44; H, 6.16; N, 4.08. Found: C, 80.12; H, 6.04; N, 3.97.

**7-(Hexylamino)-9-phenyl-6H-benzo[c]chromen-6-one (4c).** Yellow solid; mp: 94–96 °C; yield: 0.285 g, 77%; IR (neat): 3329.6, 3064.2, 2957.5, 2923.5, 1672.6, 1605.7, 1560.8, 1442.7, 1374.8, 1208.1, 1093.9  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  0.84 (t,  $J = 6.9$  Hz, 3H), 1.26–1.33 (m, 4H), 1.40 (quin,  $J = 6.9$  Hz, 2H), 1.72 (quin,  $J = 7.2$  Hz, 2H), 3.25 (t,  $J = 7.2$  Hz, 2H), 6.89 (s, 1H), 7.20–7.26 (m, 2H), 7.35–7.47 (m, 5H), 7.62 (td,  $J = 6.6, 1.2$  Hz, 2H), 8.00 (dd,  $J = 8.1, 1.5$  Hz, 1H), 8.60 (brs, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.1, 22.6, 26.9, 28.9, 31.6, 43.2, 101.8, 106.4, 108.4, 117.2, 118.8, 123.2, 124.2, 127.4, 128.5, 128.9, 130.0, 136.5, 140.9, 148.5, 151.1, 152.4, 163.2; anal. calcd for  $\text{C}_{25}\text{H}_{25}\text{NO}_2$ : C, 80.83; H, 6.78; N, 3.77. Found: C, 80.54; H, 6.65; N, 3.68.

**7-(Cyclohexylamino)-9-phenyl-6H-benzo[c]chromen-6-one (4d).** Yellow solid; mp: 219–221 °C (Lit. 223–224 °C);<sup>17</sup> yield: 0.273 g, 73%; IR (neat): 3320.9, 3066.0, 2917.7, 2850.9, 1675.3, 1609.2, 1564.2, 1446.4, 1349.5, 1287.9, 1250.5, 1207.8, 1092.1  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.33–1.52 (m, 5H), 1.61–1.70 (m, 1H), 1.75–1.92 (m, 2H), 2.04–2.19 (m, 2H), 3.50–3.62 (m, 1H), 6.88 (s, 1H), 7.25–7.40 (m, 2H), 7.41–7.54 (m, 5H), 7.67 (td,  $J = 7.8, 1.8$  Hz, 2H), 8.06 (dd,  $J = 8.1, 1.2$  Hz, 1H), 8.71 (d,  $J = 7.2$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.6, 25.8, 32.6, 50.9, 101.7, 106.3, 108.9, 117.3, 118.9, 123.2, 124.2, 127.5, 128.5, 128.9, 130.0, 136.7, 141.1, 148.6, 151.2, 151.7, 163.3; anal. calcd for  $\text{C}_{25}\text{H}_{23}\text{NO}_2$ : C, 81.27; H, 6.28; N, 3.79. Found: C, 80.95; H, 6.19; N, 3.72.

**9-Phenyl-7-(phenylamino)-6H-benzo[c]chromen-6-one (4e).** Yellow solid; mp: 210–212 °C (205–206 °C);<sup>17</sup> yield: 0.269 g, 75%; IR (neat): 3289.1, 3060.2, 3033.4, 2920.3, 1678.9, 1612.3, 1582.7, 1557.3, 1488.4, 1404.7, 1343.6, 1250.6, 1075.3  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.19 (tt,  $J = 6.9, 2.1$  Hz, 1H), 7.30–7.51 (m, 11H), 7.58–7.61 (m, 3H), 8.10 (d,  $J = 8.1$  Hz, 1H), 10.32 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  103.1, 108.8, 110.7, 117.4, 118.7, 123.3, 123.9, 124.5, 124.8, 127.4, 128.7, 128.9, 129.6, 130.3, 136.6, 139.9, 140.3, 148.4, 150.2, 151.0, 163.3; anal. calcd for  $\text{C}_{25}\text{H}_{17}\text{NO}_2$ : C, 82.63; H, 4.72; N, 3.85. Found: C, 82.51; H, 4.67; N, 3.72.

**7-(Butylamino)-9-(*p*-tolyl)-6H-benzo[c]chromen-6-one (4f).** Yellow solid; mp: 148–150 °C; yield: 0.254 g, 71%; IR (neat): 3324.0, 3036.8, 2927.9, 2838.9, 1674.8, 1559.3, 1447.9, 1397.2, 1248.9, 1206.3, 1093.6  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.00 (t,  $J = 7.2$  Hz, 3H), 1.53 (quin,  $J = 7.2$  Hz, 2H), 1.78 (quin,  $J = 7.2$  Hz, 2H), 2.44 (s, 3H), 3.32 (q,  $J = 6.6$  Hz, 2H), 6.85 (s, 1H), 7.28–7.32 (m, 4H), 7.42–7.46 (m, 2H), 7.59 (d,  $J = 7.8$  Hz, 2H), 8.06 (d,  $J = 7.8$  Hz, 1H), 8.52–8.68 (m, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.9, 20.4, 21.3, 31.0, 42.9, 101.6, 106.3, 108.2, 117.3, 118.9, 123.3, 124.2, 127.3, 129.6, 130.0, 136.5, 138.0, 138.6, 148.6, 151.2, 152.6, 163.3; anal. calcd for  $\text{C}_{24}\text{H}_{23}\text{NO}_2$ : C, 80.64; H, 6.49; N, 3.92. Found: C, 80.28; H, 6.35; N, 3.89.



**7-(Cyclohexylamino)-9-(*p*-tolyl)-6*H*-benzo[*c*]chromen-6-one (4g).** Yellow solid; mp: 136–138 °C; yield: 0.299 mg, 78%; IR (neat): 3317.8, 3022.4, 2916.4, 2849.9, 1674.5, 1608.5, 1562.7, 1444.5, 1348.7, 1250.6, 1092.3 cm<sup>-1</sup>. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 1.45 (quin, *J* = 9.9 Hz, 5H), 1.61–1.69 (m, 1H), 1.76–1.88 (m, 2H), 2.01–2.18 (m, 2H), 2.44 (s, 3H), 3.49–3.66 (m, 1H), 6.86 (s, 1H), 7.24–7.33 (m, 4H), 7.38 (d, *J* = 1.2 Hz, 1H), 7.43 (td, *J* = 7.2, 3.0 Hz, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 8.05 (dd, *J* = 7.8, 0.9 Hz, 1H), 8.70 (d, *J* = 7.2 Hz, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 21.3, 24.7, 25.9, 32.6, 50.8, 101.6, 106.1, 108.6, 107.2, 119.0, 123.2, 124.1, 127.3, 129.6, 129.9, 136.6, 138.1, 138.5, 148.5, 151.1, 151.6, 163.3; anal. calcd for C<sub>26</sub>H<sub>25</sub>NO<sub>2</sub>: C, 81.43; H, 6.57; N, 3.65. Found: C, 81.14; H, 6.47; N, 3.70.

**7-(Benzylamino)-9-(*p*-tolyl)-6*H*-benzo[*c*]chromen-6-one (4h).** Yellow solid; mp: 158–163 °C; yield: 0.324 g, 83%; IR (neat): 3337.5, 3038.2, 2920.2, 2855.4, 1684.3, 1612.0, 1578.8, 1453.5, 1345.6, 1254.0, 1114.8, 1096.0, 1045.6 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.41 (s, 3H), 4.60 (d, *J* = 5.7 Hz, 2H), 6.83 (s, 1H), 7.26–7.27 (m, 2H), 7.31 (d, *J* = 6.3 Hz, 2H), 7.35 (d, *J* = 6.0 Hz, 2H), 7.39–7.47 (m, 7H), 8.08 (d, *J* = 7.8 Hz, 1H), 9.1 (t, *J* = 5.4 Hz, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 21.2, 47.2, 102.2, 107.0, 108.9, 117.3, 118.9, 123.3, 124.3, 127.1, 127.2, 127.4, 128.8, 129.6, 130.1, 136.6, 137.7, 138.2, 138.6, 148.5, 151.2, 152.3, 163.4; anal. calcd for C<sub>27</sub>H<sub>21</sub>NO<sub>2</sub>: C, 82.84; H, 5.41; N, 3.58. Found: C, 82.48; H, 5.45; N, 3.62.

**7-(Phenylamino)-9-(*p*-tolyl)-6*H*-benzo[*c*]chromen-6-one (4i).** Yellow solid; mp: 156–160 °C; yield: 0.283 g, 75%; IR (neat): 3291.4, 3045.8, 2936.0, 1686.4, 1614.3, 1596.8, 1554.1, 1449.3, 1396.2, 1284.7, 1148.3, 1114.6 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.41 (s, 3H), 7.19 (t, *J* = 6.6 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 2H), 7.30–7.45 (m, 8H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.58 (s, 1H), 8.10 (d, *J* = 7.5 Hz, 1H), 10.31 (s, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ\* 21.3, 104.7, 110.8, 114.7, 117.8, 118.5, 123.4, 125.2, 127.3, 129.8, 130.7, 135.4, 136.6, 139.2, 150.3, 150.8, 162.6, 165.4; anal. calcd for C<sub>26</sub>H<sub>19</sub>NO<sub>2</sub>: C, 82.74; H, 5.07; N, 3.71. Found: C, 82.65; H, 5.02; N, 3.59. \*Four aromatic carbons are merged with others.

**9-(*p*-Tolyl)-7-(*p*-tolylamino)-6*H*-benzo[*c*]chromen-6-one (4j).** Yellow solid; mp: 156–160 °C; yield: 0.318 g, 81%; IR (neat): 3296.2, 3045.2, 2921.0, 1684.2, 1611.3, 1585.8, 1516.1, 1440.3, 1347.0, 1275.3, 1210.7, 1141.3, 1083.8 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.30 (s, 3H), 2.33 (s, 3H), 7.17–7.18 (m, 9H), 7.40–7.47 (m, 4H), 8.02 (d, *J* = 7.5 Hz, 1H), 10.14 (s, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 21.0, 21.2, 102.6, 108.2, 110.4, 117.4, 118.8, 123.3, 124.2, 124.4, 127.2, 129.6, 130.1, 130.2, 134.6, 136.5, 137.2, 137.4, 138.7, 148.3, 150.7, 151.1, 163.3; anal. calcd for C<sub>27</sub>H<sub>21</sub>NO<sub>2</sub>: C, 82.84; H, 5.41; N, 3.58. Found: C, 82.55; H, 5.36; N, 3.48.

**9-(*p*-Tolyl)-7-(*m*-tolylamino)-6*H*-benzo[*c*]chromen-6-one (4k).** Yellow solid; mp: 145–150 °C; yield: 0.301 g, 77%; IR (neat): 3326.1, 3030.6, 2920.6, 2851.6, 1685.6, 1613.7, 1560.6, 1515.6, 1490.0, 1399.8, 1246.1, 1106.6, 1083.1 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.38 (s, 3H), 2.41 (s, 3H), 7.0 (d, *J* = 7.2 Hz, 1H), 7.18 (m, 2H), 7.28–7.36 (m, 4H), 7.42–7.59 (m, 6H), 8.10 (d, *J* = 7.5 Hz, 1H), 10.26 (s, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 21.2, 21.5, 102.9, 108.5, 110.6, 117.4, 118.7, 120.7, 123.3, 124.4, 124.6, 125.5, 127.2, 129.3, 129.6, 130.2, 136.5, 137.4, 138.7, 139.6,

139.8, 148.2, 150.3, 151.0, 163.3; anal. calcd for C<sub>27</sub>H<sub>21</sub>NO<sub>2</sub>: C, 82.84; H, 5.41; N, 3.58. Found: C, 82.63; H, 5.29; N, 3.46.

**7-((4-Chlorophenyl)amino)-9-(*p*-tolyl)-6*H*-benzo[*c*]chromen-6-one (4l).** Yellow solid; mp: 215–220 °C; yield: 0.318 g, 77%; IR (neat): 3301.0, 3030.6, 2920.1, 2851.6, 1681.7, 1613.2, 1583.5, 1558.8, 1491.1, 1255.5, 1209.4, 1082.9 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 2.34 (s, 3H), 7.19–7.25 (m, 5H), 7.27–7.31 (m, 4H), 7.39–7.44 (m, 3H), 7.54 (s, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 10.20 (s, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ\* 20.2, 102.1, 108.0, 109.3, 116.4, 117.5, 122.2, 123.5, 123.9, 126.1, 128.6, 128.7, 129.4, 135.6, 136.1, 137.5, 137.9, 147.3, 148.7, 149.9, 162.2; anal. calcd for C<sub>26</sub>H<sub>18</sub>ClNO<sub>2</sub>: C, 75.82; H, 4.41; N, 3.40. Found: C, 75.68; H, 4.34; N, 3.33. \*One aromatic carbon is merged with others.

**7-(Hexylamino)-9-(4-methoxyphenyl)-6*H*-benzo[*c*]chromen-6-one (4m).** Yellow solid; mp: 78–85 °C; yield: 0.281 g, 70%; IR (neat): 3333.3, 2955.1, 2929.6, 2857.2, 1686.4, 1609.2, 1583.4, 1567.3, 1458.7, 1345.5, 1294.3, 1179.9, 1094.3 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 0.91 (t, *J* = 7.5 Hz, 3H), 1.36 (m, 4H), 1.49 (m, 2H), 1.78 (quin, *J* = 7.5 Hz, 2H), 3.31 (m, 2H), 3.89 (s, 3H), 6.82 (s, 1H), 7.03 (d, *J* = 8.7 Hz, 2H), 7.3 (m, 2H), 7.43 (m, 2H), 7.64 (d, *J* = 8.7 Hz, 2H), 8.06 (d, *J* = 7.5 Hz, 1H), 8.58 (t, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 14.1, 22.6, 26.9, 28.9, 31.6, 43.2, 55.4, 101.3, 106.0, 107.8, 114.3, 117.3, 118.9, 123.2, 124.1, 128.5, 129.9, 133.2, 136.4, 148.1, 151.2, 152.5, 160.1, 163.3; anal. calcd for C<sub>26</sub>H<sub>27</sub>NO<sub>3</sub>: C, 77.78; H, 6.78; N, 3.49. Found: C, 77.54; H, 6.80; N, 3.49.

**7-(Benzylamino)-9-(4-methoxyphenyl)-6*H*-benzo[*c*]chromen-6-one (4n).** Yellow solid; mp: 150–155 °C; yield: 0.313 g, 77%; IR (neat): 3337.0, 3026.4, 2920.8, 2837.2, 1683.6, 1583.5, 1565.6, 1454.1, 1403.6, 1345.1, 1294.3, 1254.1, 1179.8, 1096.2 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 3.86 (s, 3H), 4.60 (d, *J* = 5.4 Hz, 2H), 6.81 (s, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 7.30 (dd, *J* = 9.0, 2.7 Hz), 7.35 (d, *J* = 7.5 Hz, 2H), 7.39–7.44 (m, 5H), 7.51 (d, *J* = 8.7 Hz, 2H), 8.07 (d, *J* = 8.1 Hz, 1H), 9.09 (t, *J* = 5.7 Hz, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 47.2, 55.4, 101.9, 106.7, 108.5, 114.3, 117.3, 118.8, 123.2, 124.2, 127.1, 127.4, 128.5, 128.8, 130.1, 132.9, 136.5, 138.2, 148.1, 151.1, 152.2, 160.1, 163.3; anal. calcd for C<sub>27</sub>H<sub>21</sub>NO<sub>3</sub>: C, 79.59; H, 5.19; N, 3.44. Found: C, 79.30; H, 5.24; N, 3.43.

**7-(Cyclohexylamino)-9-(2-hydroxyphenyl)-6*H*-benzo[*c*]chromen-6-one (4o).** Yellow solid; mp: 200–208 °C; yield: 0.242 g, 63%; IR (neat): 3339.7, 3046.0, 2930.2, 2853.4, 1659.9, 1613.1, 1566.9, 1450.1, 1350.0, 1256.1, 1111.5 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 1.34–1.47 (m, 4H), 1.62 (m, 2H), 1.80 (m, 2H), 2.06 (m, 2H), 3.45 (quin, 1H), 5.60 (brs, 1H), 6.77 (s, 1H), 7.03–7.08 (m, 2H), 7.23–7.37 (m, 5H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H), 8.73 (d, *J* = 7.5 Hz, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 24.6, 25.7, 32.5, 50.9, 101.8, 107.6, 110.5, 116.5, 117.2, 118.5, 120.9, 123.3, 124.3, 128.0, 129.8, 129.9, 130.2, 137.1, 145.1, 151.0, 151.7, 152.8, 163.2; anal. calcd for C<sub>25</sub>H<sub>23</sub>NO<sub>3</sub>: C, 77.90; H, 6.01; N, 3.63. Found: C, 77.57; H, 6.11; N, 3.48.

**7-(Benzylamino)-9-(2-hydroxyphenyl)-6*H*-benzo[*c*]chromen-6-one (4p).** Yellow solid; mp: 214–216 °C; yield: 0.302 g, 77%; IR (neat): 3353.2, 3195.2, 2853.5, 1649.3, 1609.6, 1560.6, 1446.8, 1367.3, 1256.2, 1211.0, 1092.4 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 4.53 (d, *J* = 5.7 Hz, 2H), 5.39 (s, 1H), 6.73 (s, 1H), 7.00 (t, *J* = 7.8 Hz, 2H), 7.22–7.37 (m, 10H), 7.45 (td, *J* = 8.4, 1.5 Hz, 1H),



7.98 (dd,  $J = 8.1, 0.9$  Hz, 1H), 9.13 (t,  $J = 5.1$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  47.0, 102.6, 108.6, 110.6, 116.4, 117.4, 118.4, 121.0, 123.4, 124.5, 127.1, 127.4, 127.5, 128.9, 129.8, 130.0, 130.5, 137.2, 137.7, 145.1, 151.1, 152.4, 152.6, 163.2; anal. calcd for  $\text{C}_{26}\text{H}_{19}\text{NO}_3$ : C, 79.37; H, 4.87; N, 3.56. Found: C, 78.98; H, 4.71; N, 3.49.

**9-(2-Hydroxyphenyl)-7-(1-tolylamino)-6H-benzo[*c*]chromen-6-one (4q).** Yellow solid; mp: 228–235 °C; yield: 0.276 g, 70%; IR (neat): 3336.4, 3044.7, 2917.8, 2849.9, 1739.4, 1681.8, 1586.7, 1560.3, 1413.4, 1262.0, 1210.8  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3/\text{DMSO}-d_6$ ):  $\delta$  2.35 (s, 3H), 5.44 (s, 1H), 6.96–7.02 (m, 2H), 7.19–7.44 (m, 9H), 7.46–7.49 (m, 2H), 8.00 (d,  $J = 7.8$  Hz, 1H), 10.23 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3/\text{DMSO}-d_6$ ):  $\delta$  19.6, 100.9, 109.8, 111.9, 115.2, 115.7, 117.4, 118.4, 122.2, 123.3, 123.5, 125.9, 128.4, 128.8, 128.9, 132.6, 134.2, 135.9, 145.3, 148.1, 149.4, 153.4, 161.7; anal. calcd for  $\text{C}_{26}\text{H}_{19}\text{NO}_3$ : C, 79.37; H, 4.87; N, 3.56. Found: C, 79.09; H, 4.88; N, 3.41.

**9-(4-Chlorophenyl)-7-(cyclohexylamino)-6H-benzo[*c*]chromen-6-one (4r).** Yellow solid; mp: 136–138 °C; yield: 0.362 g, 91%; IR (neat): 3315.4, 3071.1, 2922.9, 2853.6, 1679.5, 1608.9, 1557.5, 1453.6, 1372.2, 1255.5, 1205.5, 1088.1, 1025.6  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.33–1.52 (m, 5H), 1.65–1.72 (m, 1H), 1.78–1.90 (m, 2H), 2.00–2.18 (m, 2H), 3.49–3.61 (m, 1H), 6.83 (s, 1H), 7.28–7.35 (m, 3H), 7.42–7.49 (m, 3H), 7.60 (d,  $J = 8.4$  Hz, 2H), 8.04 (dd,  $J = 8.1, 0.9$  Hz, 1H), 8.75 (d,  $J = 6.3$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.6, 25.8, 32.5, 50.9, 101.9, 105.9, 108.6, 117.3, 118.7, 123.2, 124.2, 128.7, 129.1, 130.1, 134.6, 136.9, 139.4, 147.3, 151.1, 151.6, 163.2; anal. calcd for  $\text{C}_{25}\text{H}_{22}\text{NO}_2\text{Cl}$ : C, 74.34; H, 5.49; N, 3.47. Found: C, 74.05; H, 5.46; N, 3.42.

**7-(Benzylamino)-2-methoxy-9-phenyl-6H-benzo[*c*]chromen-6-one (4s).** Yellow solid; mp: 148–150 °C; yield: 0.236 g, 57%; IR (neat): 3329.2, 3061.3, 2924.8, 2876.2, 2851.7, 1677.9, 1610.4, 1568.0, 1451.8, 1368.3, 1252.2, 1098.7  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.03 (quin,  $J = 6.3$  Hz, 2H), 3.46 (t,  $J = 6.6$  Hz, 2H), 3.87 (t,  $J = 6.0$  Hz, 2H), 6.83 (s, 1H), 7.29–7.37 (m, 5H), 7.46 (td,  $J = 8.4, 1.5$  Hz, 1H), 7.54 (s, 1H), 7.98 (dd,  $J = 8.1, 0.9$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  31.7, 39.9, 60.4, 102.3, 108.7, 110.8, 117.3, 118.6, 123.3, 124.4, 127.3, 129.9, 130.3, 131.7, 133.0, 134.6, 136.2, 138.7, 145.9, 151.1, 152.0, 163.2; anal. calcd for  $\text{C}_{22}\text{H}_{17}\text{Cl}_2\text{NO}_3$ : C, 63.78; H, 4.14; N, 3.38. Found: C, 63.46; H, 4.07; N, 3.34.

**9-(2,4-Dichlorophenyl)-7-((3-hydroxypropyl)amino)-6H-benzo[*c*]chromen-6-one (4t).** Yellow solid; mp: 165–170 °C; yield: 0.289 g, 71%; IR (neat): 3342.39, 3056.4, 2933.6, 2840.2, 1583.5, 1565.7, 1454.0, 1403.6, 1344.9, 1294.2, 1179.9, 1096.4  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.86 (s, 3H), 4.59 (d,  $J = 5.4$  Hz, 2H), 6.80 (s, 1H), 6.97 (d,  $J = 8.7$  Hz, 2H), 7.28–7.44 (m, 9H), 7.50 (d,  $J = 8.7$  Hz, 2H), 8.06 (d,  $J = 8.1$  Hz, 1H), 9.09 (brs, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  47.2, 55.4, 101.9, 106.7, 108.5, 114.3, 117.3, 118.8, 123.2, 124.2, 127.2, 127.4, 128.5, 128.8, 130.0, 132.9, 136.5, 138.3, 148.0, 151.1, 152.3, 160.1, 163.3; anal. calcd for  $\text{C}_{27}\text{H}_{21}\text{NO}_3$ : C, 79.59; H, 5.19; N, 3.44. Found: C, 79.34; H, 5.12; N, 3.37.

**2-Bromo-7-(cyclohexylamino)-9-phenyl-6H-benzo[*c*]chromen-6-one (4u).** Yellow solid; mp: 178–183 °C; yield: 0.300 g, 67%; IR (neat): 3373.5, 3018.2, 2930.2, 2853.9, 1689.6, 1612.3, 1567.8, 1498.0, 1409.2, 1254.5, 1188.8, 1099.6  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,

$\text{CDCl}_3$ ):  $\delta$  1.25–1.51 (m, 5H), 1.60–1.70 (m, 1H), 1.81–1.82 (m, 2H), 2.09–2.12 (m, 2H), 3.54 (m, 1H), 6.89 (s, 1H), 7.18 (d,  $J = 8.7$  Hz, 1H), 7.27 (d,  $J = 4.8$  Hz, 1H), 7.45–7.54 (m, 4H), 7.66 (dd,  $J = 8.1, 1.4$  Hz, 2H), 8.13 (d,  $J = 2.1$  Hz, 1H), 8.67 (d,  $J = 7.5$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.6, 25.8, 32.5, 50.9, 101.3, 106.3, 109.5, 117.1, 119.0, 120.8, 126.0, 127.4, 128.7, 129.0, 132.7, 135.3, 140.3, 148.8, 150.0, 151.7, 162.7; anal. calcd for  $\text{C}_{25}\text{H}_{22}\text{BrNO}_2$ : C, 66.97; H, 4.95; N, 3.12. Found: C, 66.76; H, 4.87; N, 3.06.

**2-Bromo-9-phenyl-7-(*p*-tolylamino)-6H-benzo[*c*]chromen-6-one (4v).** Yellow solid; mp: 205–209 °C; yield: 0.297 g, 65%; IR (neat): 3301.0, 3030.6, 2921.1, 2855.4, 1688.3, 1611.5, 1586.8, 1509.2, 1459.2, 1411.8, 1252.3, 1113.5, 1074.7  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.38 (s, 3H), 7.20–7.26 (m, 5H), 7.35 (d,  $J = 1.5$  Hz, 1H), 7.41–7.49 (m, 4H), 7.53–7.59 (m, 3H), 8.18 (d,  $J = 2.1$  Hz, 1H), 10.16 (s, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  21.0, 102.4, 108.5, 111.2, 117.4, 119.1, 120.6, 124.4, 126.1, 127.3, 128.8, 129.1, 130.2, 133.0, 135.0, 135.2, 136.8, 140.0, 148.6, 149.9, 150.9, 162.7; anal. calcd for  $\text{C}_{26}\text{H}_{18}\text{BrNO}_2$ : C, 68.43; H, 3.98; N, 3.07. Found: C, 68.07; H, 4.04; N, 2.99.

**7-(Cyclohexylamino)-9-(furan-2-yl)-6H-benzo[*c*]chromen-6-one (4w).** Yellow solid; mp: 160–164 °C; yield: 0.241 g, 67%; IR (neat): 3320.0, 2930.6, 2854.3, 1684.1, 1615.2, 1566.8, 1498.8, 1453.6, 1375.4, 1255.4, 1211.9, 1095.1, 1019.2  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.25–1.69 (m, 6H), 1.83 (m, 2H), 2.10 (m, 2H), 3.57 (m, 1H), 6.56 (dd,  $J = 3.3, 1.8$  Hz, 1H), 6.88 (d,  $J = 3.3$  Hz, 1H), 7.02 (s, 1H), 7.30 (d,  $J = 8.1$  Hz, 2H), 7.44 (td,  $J = 7.2, 1.5$  Hz, 1H), 7.50 (s, 1H), 7.57 (d,  $J = 1.5$  Hz, 1H), 8.07 (d,  $J = 7.2$  Hz, 1H), 8.71 (d,  $J = 5.4$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.6, 25.8, 32.6, 50.8, 101.6, 102.5, 104.7, 108.0, 112.1, 117.3, 118.8, 123.3, 124.1, 130.0, 136.8, 136.9, 143.3, 151.1, 151.7, 153.2, 163.1; anal. calcd for  $\text{C}_{23}\text{H}_{21}\text{NO}_3$ : C, 76.86; H, 5.89; N, 3.90. Found: C, 76.55; H, 5.75; N, 3.83.

**7-(Cyclohexylamino)-9-(thiophen-2-yl)-6H-benzo[*c*]chromen-6-one (4x).** Yellow solid; mp: 154–160 °C; yield: 0.259 g, 69%; IR (neat): 3319.6, 2930.3, 2853.8, 1683.8, 1609.7, 1570.6, 1458.2, 1358.53, 1255.1, 1143.5, 1094.6  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.43 (m, 4H), 1.62–1.73 (m, 2H), 1.83 (m, 2H), 2.14 (m, 2H), 3.55 (brs, 1H), 6.91 (s, 1H), 7.16 (m, 1H), 7.31 (d,  $J = 7.5$  Hz, 2H), 7.42–7.50 (m, 4H), 8.04 (d,  $J = 7.5$  Hz, 1H), 8.71 (d,  $J = 6.9$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  24.6, 25.8, 32.5, 50.9, 101.8, 104.7, 107.1, 117.3, 118.7, 123.2, 124.2, 125.0, 126.5, 128.2, 130.1, 136.9, 141.1, 143.8, 151.2, 151.6, 163.1; anal. calcd for  $\text{C}_{23}\text{H}_{21}\text{NO}_2\text{S}$ : C, 73.57; H, 5.64; N, 3.73. Found: C, 73.32; H, 5.61; N, 3.69.

**7-(Benzylamino)-9-(thiophen-2-yl)-6H-benzo[*c*]chromen-6-one (4y).** Yellow solid; mp: 158–165 °C; yield: 0.272 g, 71%; IR (neat): 3346.2, 3032.6, 2918.1, 2851.6, 1684.1, 1610.5, 1569.6, 1453.8, 1261.8, 1094.3  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  4.59 (d,  $J = 5.7$  Hz, 2H), 6.88 (s, 1H), 7.11 (t,  $J = 4.8$  Hz, 1H), 7.28–7.49 (m, 11H), 8.05 (d,  $J = 7.8$  Hz, 1H), 9.11 (t,  $J = 4.8$  Hz, 1H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  47.2, 102.4, 105.6, 107.3, 117.3, 118.5, 123.3, 124.3, 125.1, 126.7, 127.2, 127.4, 128.3, 128.8, 130.3, 136.8, 138.1, 141.1, 143.5, 151.2, 152.3, 163.1; anal. calcd for  $\text{C}_{24}\text{H}_{17}\text{NO}_2\text{S}$ : C, 75.17; H, 4.47; N, 3.65. Found: C, 74.93; H, 4.40; N, 3.64.



## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

Financial support from the Department of Science and Technology-Science and Engineering Research Board, DST-SERB (No. EMR/2016/001619 & EMR/2016/002485) and MICINN (RTI2018-097662-B-I00) is gratefully acknowledged.

## Notes and references

- For reviews on natural 6*H*-benzo[*c*]chromen-6-ones and their biological activities, see: (a) Ya. L. Garazd and M. M. Garazd, *Chem. Nat. Compd.*, 2016, **52**, 1–18; (b) Z. Mao, W. Sun, L. Fu, H. Luo, D. Lai and L. Zhou, *Molecules*, 2014, **19**, 5088–5108.
- (a) T. Tanahashi, M. Kuroishi, A. Kuwahara, N. Nagakura and N. Hamada, *Chem. Pharm. Bull.*, 1997, **45**, 1183–1185; (b) E. Hormazabal, G. Schmeda-Hirschmann, L. Astudillo, J. Rodriguez and C. Theoduloz, *Z. Naturforsch., C: J. Biosci.*, 2005, **60**, 11–21.
- (a) J. Xiao, Q. Zhang, Y.-Q. Gao, J.-J. Tang, A.-L. Zhang and J.-M. Gao, *J. Agric. Food Chem.*, 2014, **62**, 3584–3590; (b) M. H. Tao, Y.-C. Chen, X.-Y. Wei, J.-W. Tan and W.-M. Zhang, *Helv. Chim. Acta*, 2014, **97**, 426–430; (c) S. Liu, Y. Dong, Y. Li, L. Bao, H. Liu and H. Li, *Fitoterapia*, 2014, **91**, 9–14; (d) H. Raistrick, C. E. Stickings and R. Thomas, *Biochem. J.*, 1953, **55**, 421–433.
- (a) D. J. Hart and A. Mannino, *Tetrahedron*, 1996, **52**, 3841–3856; (b) A. D. Patten, N. H. Nguyen and S. J. Danishefsky, *J. Org. Chem.*, 1988, **53**, 1003–1007; (c) D. M. Balitz, F. A. O'Herron, J. Bush, D. M. Vyas, D. E. Nettleton, R. E. Grulich, W. T. Bradner, T. W. Doyle, E. Arnold and J. J. Clardy, *Antibiotics*, 1981, **34**, 1544–1555.
- (a) X. Meng, Z. Mao, J. Lou, L. Xu, L. Zong, Y. Peng, L. Zhou and M. Wang, *Molecules*, 2012, **17**, 11303–11314; (b) T. Matumoto, T. Hosoya and H. Shigemori, *Heterocycles*, 2010, **81**, 1231–1237.
- P. Bhattacharya, S. M. Mandal and A. Basak, *Eur. J. Org. Chem.*, 2016, 1439–1448.
- For a review, see: O. Mazimba, *Turk. J. Chem.*, 2016, **40**, 1–27.
- For selected recent examples of the synthesis of 6*H*-benzo[*c*]chromen-6-ones involving the generation of the lactone ring, see: (a) T. Morack, J. B. Metternich and R. Gilmour, *Org. Lett.*, 2018, **20**, 1316–1319; (b) Q. Yang, Z. Jia, L. Li, L. Zhang and S. Luo, *Org. Chem. Front.*, 2018, **5**, 237–241; (c) K. Subramanian, S. L. Yedage and B. M. Bhanage, *Adv. Synth. Catal.*, 2018, **360**, 2511–2521; (d) X.-Z. Tao, J.-J. Dai, J. Z. J. Xu and H.-J. Xu, *Chem.–Eur. J.*, 2018, **24**, 6932–6935; (e) L. Zhang, Z. Zhang, J. Hong, J. Yu, J. Zhang and F. Mo, *J. Org. Chem.*, 2018, **83**, 3200–3207; (f) A. Shao, J. Zhan, N. Li, C.-W. Chiang and A. Lei, *J. Org. Chem.*, 2018, **83**, 3582–3589; (g) P. D. Q. Dao, S. L. Ho, H.-J. Lim and C. S. Cho, *J. Org. Chem.*, 2018, **83**, 4140–4146; (h) L. Lia, Q. Yang, Z. Jia and S. Luo, *Synthesis*, 2018, **50**, 2924–2929; (i) Y. Wang, J.-Y. Gu and Z.-J. Shi, *Org. Lett.*, 2017, **19**, 1326–1329; (j) S. L. Yedage and B. M. Bhanage, *J. Org. Chem.*, 2017, **82**, 5769–5781; (k) J. Zhang, D. Shi, H. Zhang, Z. Xu, H. Bao, H. Jin and Y. Liu, *Tetrahedron*, 2017, **73**, 154–163; (l) L. Huang and D. J. Weix, *Org. Lett.*, 2016, **18**, 5432–5435; (m) R. Oketani, T. Miyake, S. Jinnai, T. Fukui, H. Tsujimoto, M. Matsumura and S. Higashida, *Chem. Lett.*, 2016, **45**, 801–803; (n) P. Bhattacharya, S. M. Mandal and A. Basak, *Eur. J. Org. Chem.*, 2016, 1439–1448; (o) K. Kudo and N. Yamamoto, *Org. Process Res. Dev.*, 2015, **19**, 309–314; (p) S. Luo, F.-X. Luo, X.-S. Zhang and Z.-J. Shi, *Angew. Chem., Int. Ed.*, 2013, **52**, 10598–10601.
- C. Mou, T. Zhu, P. Zheng, S. Yang, B.-A. Song and Y. R. Chi, *Adv. Synth. Catal.*, 2016, **358**, 707–712.
- I. R. Pottie, P. R. Nandaluru, W. L. Benoit, D. O. Miller, L. N. Dawe and G. J. Bodwell, *J. Org. Chem.*, 2011, **76**, 9015–9030.
- Y. He, X. Zhang and X. Fan, *Asian J. Org. Chem.*, 2014, **3**, 1284–1291.
- T. N. Poudel and Y. R. Lee, *Org. Biomol. Chem.*, 2014, **12**, 919–930.
- I. B. Masesane and O. Mazimba, *Bull. Chem. Soc. Ethiop.*, 2014, **28**, 289–294.
- V. Sridharan and J. C. Menéndez, *Org. Lett.*, 2008, **10**, 4303–4306.
- For a review on cerium(IV) ammonium nitrate as a catalyst in organic synthesis, see: V. Sridharan and J. C. Menéndez, *Chem. Rev.*, 2010, **110**, 3805–3849.
- D. Rocchi, J. F. González, J. Gómez-Carpintero, V. González-Ruiz, M. A. Martín, V. Sridharan and J. C. Menéndez, *ACS Comb. Sci.*, 2018, **20**, 722–731.
- S. Yaragorla and R. Dada, *ACS Omega*, 2017, **2**, 4859–4869.
- For the generation of  $\beta$ -enaminones *via* CAN catalyzed reaction, see: V. Sridharan, C. Avendaño and J. C. Menéndez, *Synlett*, 2007, 0881–0884.
- For selected examples of  $\beta$ -enaminone formation-initiated multicomponent reactions from our group, see: (a) V. Estévez, V. Sridharan, S. Sabaté, M. Villacampa and J. C. Menéndez, *Asian J. Org. Chem.*, 2016, **5**, 652–662; (b) T. Vivekanand, P. Vinoth, B. Agieshkumar, N. Sampath, A. Sudalai, J. C. Menéndez and V. Sridharan, *Green Chem.*, 2015, **17**, 3415–3423; (c) P. Vinoth, P. S. R. Prasad, T. Vivekanand, C. U. Maheswari, S. Nagarajan, J. C. Menéndez and V. Sridharan, *RSC Adv.*, 2015, **5**, 81881–81888; (d) G. Tenti, E. Parada, R. León, J. Egea, S. Martínez-Revelles, A. M. Briones, V. Sridharan, M. G. López, M. T. Ramos and J. C. Menéndez, *J. Med. Chem.*, 2014, **57**, 4313–4323; (e) P. A. Suryavanshi, V. Sridharan, S. Maiti and J. C. Menéndez, *Chem.–Eur. J.*, 2014, **20**, 8791–8799; (f) P. A. Suryavanshi, V. Sridharan and J. C. Menéndez, *Chem.–Eur. J.*, 2013, **19**, 13207–13215; (g) P. A. Suryavanshi, V. Sridharan and J. C. Menéndez, *Tetrahedron*, 2013, **69**, 5401–5406.

