# Organic & **Biomolecular Chemistry**

## PAPER

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## An advanced and novel one-pot synthetic method for diverse benzo[c]chromen-6-ones by transitionmetal free mild base-promoted domino reactions of substituted 2-hydroxychalcones with $\beta$ -ketoesters and its application to polysubstituted terphenyls\*

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Novel and efficient one-pot syntheses of a variety of benzo[c]chromen-6-one derivatives were accomplished using Cs<sub>2</sub>CO<sub>3</sub>-promoted reactions between substituted 2-hydroxychalcones and  $\beta$ -ketoesters. These reactions involved domino Michael addition/intramolecular aldol/oxidative aromatization/lactonization and provided a rapid synthetic route for the production of biologically interesting novel benzo[c]chromen-6-one molecules bearing several different substituents on benzene rings. As an application of this methodology, several synthesized benzo[c]chromen-6-ones were transformed into highly functionalized novel terphenyls.

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#### 30 Introduction

Domino reactions have emerged as one of the most effective and powerful tools for the synthesis of a range of complex target molecules in organic and natural product synthesis.<sup>1</sup> In particular, they are very useful to generate a variety of new compounds which have biological and pharmacological activities.2

Molecules bearing benzo[c]chromen-6-one and its derivatives are extensively distributed in nature (Fig. 1).<sup>3</sup> Some of 40 these molecules exhibit biologically and pharmacologically important antitumor and antibiotic activities,<sup>4</sup> promote endothelial cell proliferation, and inhibit oestrogen receptor growth activities.<sup>5</sup> Benzo[c]chromen-6-ones have also been used as intermediates for the synthesis of pharmaceutically valuable 45 compounds, such as progesterone, androgen, and glucocorticoid receptor agonists.<sup>6</sup> Furthermore, some of the known benzo[c]chromen-6-one derivatives have promising optical properties as blue-green fluorescing dyes, which is rarer than fluorescence at other wavelengths.<sup>7</sup> In addition, benzo[c]chromen-6-one derivatives are present in many foods, such as citrus

9 R<sup>5</sup>=I, R<sup>6</sup>=CH<sub>3</sub> gilvocarcin M 10 R<sup>5</sup>=I, R<sup>6</sup>=CH=CH<sub>2</sub> gilvocarcin V 11 R<sup>5</sup>=II, R<sup>6</sup>=CH=CH<sub>2</sub> ravidomycin 12 R<sup>5</sup>=III, R<sup>6</sup>=CH=CH<sub>2</sub> chrysomycin 12 R<sup>5</sup>=III, R<sup>6</sup>=CH=CH<sub>2</sub> chrysomycin OF HC όн /cin B =111 **14** R<sup>5</sup>=H, R<sup>6</sup>=CH<sub>3</sub> defucogivocarcin w **15** R<sup>5</sup>=H, R<sup>6</sup>=CH=CH<sub>2</sub> defucogivocarcin V 7 verrulactone A 8 verrulactone B Fig. 1 Selected naturally occurring molecules bearing benzo[c]chromen-6-one moiety.

fruits, herbs, and vegetables.<sup>8</sup> For example, autumnariol (1) was isolated from the bulbs of Eucomis autumnalis Gerab. (Liliaceae).<sup>9a</sup> Alternariol (2), another benzo[c]chromen-6-one 50 derivative, is an important metabolite of toxin-producing Alternaria fungi, which causes significant crop losses by fouling of tomatoes, apples, and other fruits.<sup>9b</sup> Interestingly, alternariol (2) has been also shown to have antiviral, antimicrobial, anticancer, and cytotoxic activities.<sup>9c-e</sup> Palmariols A (3) and B (4)55 were isolated from discomycete Lachnumpalmae and exhibited antimicrobial, antinematodal, and acetylcholinesterase inhibitory activities.<sup>9f,g</sup> Graphislactones A (5) and B (6) were isolated



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School of Chemical Engineering, Yeungnam University, Gyeongsan 712-749, Republic of Korea. E-mail: yrlee@yu.ac.kr; Fax: +82-53-810-4631; Tel: +82-53-810-2529  $\dagger\,Electronic$  supplementary information (ESI) available: Depiction of  $^1\text{H},\ ^{13}\text{C}$ NMR and HRMS spectra for all products 16-45 and 49-54, and CIF data of 26. CCDC 958927. For ESI and crystallographic data in CIF or other electronic Q3 format see DOI: 10.1039/c3ob41800f

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from the lichen *Graphisscripta* var. *pulverrulenta*.<sup>10*a*-*f*</sup> Graphislactone A (5) acts as an antioxidant and free radical scavenger,<sup>11</sup> and was found to be active against the SW1116 cell line and an active inhibitor of AChE.<sup>10*e*</sup> Verrulactones A (7) and B (8) were isolated from a culture broth of the fungal strain *Penicillium verruculosum* F375,<sup>10*a*-*f*</sup> and inhibited *Staphylococcus aureus* enoyl-ACP reductase with an IC<sub>50</sub> of 0.92 µM and exhibited antibacterial activity against *S. aureus* and MRSA with MICs of 8 µg mL<sup>-1.12</sup> Gilvocarcins M (9) and V (10), ravidomycin (11), and chrysomycins A (12) and B (13), which have a sugar nucleus at the C-4 position, and defucogivocarcines M (14) and V (15), which do not bear the sugar moiety, were isolated from other *Streptomyces* species found to be strong natural anticancer agents, and to exhibit important and potent antibacterial, antibiotic, and antitumor activities.<sup>13</sup>

Given the importance of these biological and pharmacological activities, several synthetic methods have been devised to produce benzo[*c*]chromen-6-one derivatives. Of these methods, the most useful one involves a Suzuki-Miyaura cross-coupling 20 reaction followed by metal or Lewis acid-mediated lactonization of ester and methoxy groups (eqn (1), Scheme 1).<sup>14</sup> Recently, a new reaction involving a microwave-assisted Diels-Alder reaction between 4-cyanocoumarin and 1-oxygenated 25 dienes followed by elimination and aromatization with a strong base was also described (eqn (2)).<sup>15</sup> However, this synthetic approach included two-step reactions and required purification of the intermediate. In addition, the starting materials used for this transformation were synthesized from the corres-30 ponding materials in two or more steps. Very recently, novel one-pot reactions were devised for the synthesis of benzo[c]chromen-6-one derivatives by palladium bis(acetoacetonate)/ CuCl-catalyzed decarboxylative cross-coupling and lactonization,<sup>16</sup> or by palladium acetate-catalyzed Suzuki-Miyaura coup-35 ling followed by oxidative lactonization (eqn (3) and (4)).<sup>17</sup> However, to complete these reactions, relatively expensive catalysts, reagents, and ligands are needed. Thus, a mild, general, and efficient one-pot synthetic route for benzo[c]chromen-6one derivatives using inexpensive catalysts and reagents has 40 vet to be devised.

To the best of our knowledge, no previous report has been issued on the synthesis of tricyclic benzo[c]chromen-6-one

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derivatives *via* domino Michael addition/intramolecular aldol/ oxidative aromatization/lactonization reactions between substituted 2-hydroxychalcones and  $\beta$ -ketoesters.

We report herein a novel and efficient means for synthesizing benzo[c]chromen-6-one derivatives from readily available substituted 2-hydroxychalcones and  $\beta$ -ketoesters *via* domino Michael/intramolecular aldol/aromatization/lactonization reactions (Scheme 2).

### **Results and discussion**

20 To afford benzo[c] chromen-6-one 16, the reaction between 2-hydroxychalcone (1a) and ethyl acetoacetate (2a) was first examined under several conditions (Table 1). Treatment of 1a with 2a in the presence of 2 equivalents of DBU in refluxing toluene for 7 h afforded product 16 in 50% yield, but using 25 sodium methoxide in refluxing methanol for 12 h, 16 was produced in 40% yield. Using K<sub>2</sub>CO<sub>3</sub> and Cs<sub>2</sub>CO<sub>3</sub>, the desired product 16 was produced at higher yields. For example, reaction with 2 equivalents of  $K_2CO_3$  in refluxing toluene for 6 h provided product 16 in 66% yield, whereas reaction with 30 2 equivalents of Cs<sub>2</sub>CO<sub>3</sub> afforded 16 in 71% yield. In recent years, Cs<sub>2</sub>CO<sub>3</sub> has been widely used as an excellent base for a variety of transformations in organic synthesis.<sup>18</sup> Importantly, we found that Cs<sub>2</sub>CO<sub>3</sub> is more efficient than other bases for the production of 16 in terms of yield and reaction time. 35 However, using one equivalent or a catalytic amount of  $Cs_2CO_3$ (0.1 eq.), the desired product was produced at lower yields. Reactions in water or methanol under reflux conditions did not provide the desired products. The structure of 16 was 40 determined by analyzing spectral data. The <sup>1</sup>H NMR spectrum of 16 showed a single OH peak at  $\delta$  11.30 ppm in downfield due to hydrogen bonding with the ester carbonyl group, and



Scheme 1 Reported synthetic approaches for benzo[c]chromen-6-ones.

Table 1Reaction of 2-hydroxychalcone (1a) with ethyl acetoacetate45(2a) under several conditions

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	$H_{OH}$ $H_{Ia}$ $H_{OH}$ $H_{Ia}$ $H_{OH}$ $H_{Ia}$ $H_{OH}$ $H_{Ia}$ $H$					
Entry	Base	Solvent	Condition	Yield (%)		
1	DBU (2 eq.)	Toluene	Reflux, 7 h	50		
2	NaOMe (2 eq.)	MeOH	Reflux, 12 h	40		
3	$K_2CO_3$ (2 eq.)	Toluene	Reflux, 6 h	66		
4	$Cs_2CO_3$ (2 eq.)	Toluene	Reflux, 2 h	71	55	
5	$Cs_2CO_3$ (1 eq.)	Toluene	Reflux, 6 h	55		
6	$Cs_2CO_3$ (0.1 eq.)	Toluene	Reflux, 12 h	15		
7	$Cs_2CO_3$ (2 eq.)	Water	Reflux, 12 h	0		
8	$Cs_2CO_3$ (2 eq.)	MeOH	Reflux, 12 h	0		

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two single peaks at  $\delta$  7.69 and 7.20 ppm associated with two aromatic peaks on the benzo[*c*]chromen-6-one ring. The structure was further confirmed by <sup>13</sup>C NMR spectrum, which showed the expected carbonyl peak at  $\delta$  162.6 ppm due to the ester. In addition, the IR spectrum of **16** contained an ester carbonyl absorption at 1684 cm<sup>-1</sup>.

To prepare a variety of benzo[c]chromen-6-one derivatives, 1 additional reactions between substituted 3-(2-hydroxyphenyl)prop-2-en-1-ones and several  $\beta$ -ketoesters were carried out under optimized reaction conditions. Results are summarized in Table 2. Reactions between **1a** and ethyl-3-oxopentanoate 5 (**2b**), methyl-3-oxo-4-phenyl butanoate (**2c**) or diethyl-3-

Entry	Chalcone	β-Ketoester	Time (h)	Product	Yield (%)
1	O I I I I I I		2	0 OH 0 H 17 17	51
2	1a	C O O 2c OMe	2		58
3	1a		2		60
4	O Ab OH		2	O OH	50
5		2a	2		70
6	10	2b	2		52
7	Br Collection	2a	3		55
8	1d 1d	2c	3		63
9		2a	2	O OH	70
10	1e	2b	3		54
11	1e	2d	3		62

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Entry	Chalcone	β-Ketoester	Time (h)	Product	Yield (%
12	MeO OH OMe	2a	2	MeO OH OME	72
13	1f	2b	2	MeO OH	54
14	1f	2c	3	MeO OH	60
15	O Ig OH	2a	2		69
16	D L D H OH OMe	2b	2	O OH O H OH 32 OMe	55
17		2a	3	O OH O J J J J J J J J J J J J J J J J J J J	70
18	1i	2c	3	O OH O OH 34	63
19		2a	3		71
20	1j	2b	3		53
21	1j	2c	3		65
22		2a	2		73
23	1k	2b	2	Br O O H O H S S	50
24	1k	2d	2		64

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Entry	Chalcone	β-Ketoester	Time (h)	Product	Yield (%)
25	OH CON	2a	2	O OH	63
26	1) 1]	2b	3		51
27	11	2c	3		50
28	C CH	2a	2		72
29	1m 1m	2c	2		61

25 oxopentanedioate (2d) in the presence of 2 equivalents of Cs<sub>2</sub>CO<sub>3</sub> in refluxing toluene for 2 h provided the desired products 17-19 in 51, 58, and 60% yield, respectively (entries 1-3). The reaction of chalcone 1b with a methyl group on the 2-propen-1-one skeleton was also successful. Treatment of 1b 30 with 2b in the presence of  $Cs_2CO_3$  in refluxing toluene for 2 h afforded product 20 in 50% yield (entry 4). To investigate the influence of substituents on reactivities, the effects of a number of 2-hydroxychalcones (1c-1h) bearing electron-donating or -withdrawing groups on the benzene ring were next 35 examined. Reactions between 1c bearing a methyl group on the phenolic moiety and 2a or 2b afforded products 21-22 in 70 and 52% yield, respectively, whereas those of 1d with an electron-withdrawing group on the phenolic ring provided 23-24 in 55 and 63% yield, respectively (entries 5-8). Reactions 40 of chalcones 1e and 1f bearing electron-donating groups on the two benzene rings were also examined. Treatment of 1e with 2a, 2b, or 2d provided compounds 25-27 in 70, 54, and 62% yield, respectively, whereas treatment of 1f with 2a-2c gave products 28-30 in 72, 54, and 60% yield, respectively 45 (entries 9-14). Reactions of chalcones 1g and 1h bearing substituents on the 1-phenyl ring with 2a or 2b gave products 31-32 in 69 and 55% yield, respectively (entries 15-16). Importantly, when (E)-3-(2-hydroxyphenyl)-1-(pyridine-3-yl)prop-2-en-50 1-one (1i), (E)-3-(2-hydroxyphenyl)-1-(2,5-dimethylfuran-3-yl)prop-2-en-1-one (1j), (*E*)-3-(2-hydroxyphenyl)-1-(2,5or dimethylthiophen-3-yl)prop-2-en-1-one (1k) were used, the desired products 33-40 were produced in 50-73% yield (entries 17-24). Reactions between (E)-3-(2-hydroxyphenyl)-1-55 (naphthalene-2-yl)prop-2-en-1-one (1l) and  $\beta$ -ketoesters were also successful. When 1l was treated with 2a, 2b, or 2c, products 41-43 were produced in 63, 51, and 50% yield, respecthydroxyphenyl)prop-2-en-1-one (**1m**) was used, compounds **44** 25 and **45** were obtained in 72 and **61%** yield, respectively (entries 28–29). These reactions provided a rapid route for synthesizing a variety of benzo[c]chromen-6-one derivatives bearing different substituents on the benzene ring. The structures of the synthesized compounds **16–45** were unambiguously confirmed by X-ray diffraction analysis of compound **26** (Fig. 2). Interestingly, the unit of the compound **26** contains two same molecules.

A proposed mechanism for the  $Cs_2CO_3$ -mediated domino reactions used to produce **16** is depicted in Scheme 3. In basic medium, the enolate of **2a** first attacks the unsaturated  $\beta$ -carbon to the carbonyl group of **1a** to give intermediate **46**, which undergoes an intramolecular aldol reaction followed by



Fig. 2 X-ray structure of compound 26 containing two molecules in a unit.

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(E)-1-cyclopropyl-3-(2-

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Scheme 3 Proposed mechanism for the formation of 7-hydroxy-9phenyl-6H-benzo[c]chromen-6-one (16) via domino reactions.

oxidative aromatization to form intermediate **48**. Finally, the lactonization of **48** under basic conditions results in **16**.

As an example of this methodology, several synthesized 15 benzo[c]chromen-6-ones were converted into biologically and physically interesting polysubstituted terphenyls. Molecules bearing the terphenyl moiety are found in a variety of natural products<sup>19</sup> and exhibit a number of potent biological properties, which include antioxidant, neuroprotective, cytotoxic, 20 antithrombotic, and anticoagulant activities.<sup>20</sup> In addition, these molecules play a significant role in the fields of optical materials, liquid crystals, spacers in catenane, and porphyrin chemistry.<sup>21</sup> Because of their important biological and physical properties, a number of synthetic methods have been 25 devised to produce terphenyls.<sup>22</sup> These reactions typically included aryl zinc reagents with functionalized biphenyl nonaflates,<sup>23</sup> Grignard reagents containing dihalobenzenes, and triazene-substituted arylboronic esters.<sup>24</sup> Recently, other meth-30 odologies using Suzuki cross-coupling reactions between dihalobenzenes and arylboronic acids,<sup>25</sup> the gold-catalyzed cycloaromatization of dienynes,<sup>26</sup> DMEDA-catalyzed direct C-H arylation of unactivated benzenes,<sup>27</sup> and rhodium-catalyzed formal [2 + 2 + 2] cycloaddition reactions of tethered die-35 nynes containing 1-alkynylphosphine sulfides have been described.<sup>28</sup> Although a number of methods have been

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reported for the synthesis of terphenyls, synthetic methods are 1 still required for the production of polysubstituted terphenyls.

The conversions of several synthesized benzo[*c*]chromen-6ones into substituted terphenyls were also attempted, as shown in Table 3. Treatment of **20** with methyl iodide in the presence of KOH in wet DMSO at room temperature for 2 h provided **49** in 70% yield. Similarly, reactions of **23**, **30**, **39**, **42**, and **45** with methyl iodide also provided the desired polysubstituted terphenyls **50–54** in 78–87% yield. Importantly, these reactions rapidly provided various terphenyls bearing substituents, such as, –Br, –Me, –COOMe, –OMe, aryl, cyclopropyl, and furyl on their benzene rings.

### Conclusions

We described the Cs<sub>2</sub>CO<sub>3</sub>-promoted one-pot synthesis of biologically interesting benzo[c]chromen-6-one derivatives starting from substituted 2-hydroxychalcones and  $\beta$ -ketoesters. These reactions were accomplished by domino Michael addition/ intramolecular aldol/oxidative aromatization/lactonization. The described methodology has the advantages of requiring mild reaction conditions and inexpensive non-transition metals and domino one-pot reactions. In particular, the synthesized molecules were readily converted under basic conditions into biologically interesting novel terphenyls bearing different substituents on their benzene rings.

### Experimental

All experiments were carried out under open air without using any inert gas protection.  $\beta$ -Ketoesters (**2a-d**) were purchased from Sigma-Aldrich. Merck precoated silica gel plates (Art. <sup>35</sup> 5554) with a fluorescent indicator were used for analytical

 Table 3
 Conversion of benzo[c]chromen-6-ones to polysubstituted terphenyls
 49–54



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TLC. Flash column chromatography was performed using silica gel 9385 (Merck). Melting points were determined with micro-cover glasses on a Fisher-Johns apparatus and are uncorrected. <sup>1</sup>H NMR spectra were recorded on a Varian-VNS (300 MHz) spectrometer in CDCl<sub>3</sub> using 7.24 ppm as the solvent chemical shift. <sup>13</sup>C NMR spectra were recorded on a Varian-VNS (75 MHz) spectrometer in CDCl<sub>3</sub> using 77.0 ppm as the solvent chemical shift. IR spectra were recorded on a JASCO FTIR 5300 spectrophotometer. High resolution mass (HRMS) were obtained with a JEOL JMS-700 spectrometer at the Korea Basic Science Institute.

### General procedure for the synthesis of 2-hydroxychalcones

15 **(1a-m)** 

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To a solution of ketones (20.0 mmol) in ethanol (50 mL) were added KOH (5.6 g, 100.0 mmol) and salicylaldehydes (20.0 mmol) at room temperature. The reaction mixture was stirred at room temperature for 48 h. Evaporation of ethanol, addition of water (50 ml) and 1 N HCl (50 mL), extraction with EtOAc ( $3 \times 50$  mL), washing with brine (50 mL), and removal of the solvent followed by flash column chromatography on silica gel using hexane–EtOAc (10:1) gave 2-hydroxychalcones (1a-1m) in the range of 53–84% yield.

### General procedure for the synthesis of benzo[*c*]chromen-6-ones (16–45)

To a solution of 2-hydroxychalcone compounds 1a-1m
(1.0 mmol) and β-ketoesters 2a-2d (1.5 mmol) in toluene
(4 mL) was added Cs<sub>2</sub>CO<sub>3</sub> (2.0 mmol). The reaction mixture was refluxed in open air for 2 h. Then the solvent was evaporated in a rotary evaporator under reduced pressure to give the residue. The residue was purified by flash column chromatography on silica gel to give the products. Characterization data for all compounds 16-45 are as follows.

7-Hydroxy-9-phenyl-6*H*-benzo[*c*]chromen-6-one (16). Reaction of 1a (224 mg, 1.0 mmol) and β-ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 16 (204 mg, 71%) as a solid: mp 213–215 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.30 (1H, s), 8.02 (1H, d, *J* = 7.8 Hz), 7.68 (1H, s), 7.60 (2H, d, *J* = 6.9 Hz), 7.44–7.36 (4H, m), 7.31–7.27 (2H, m), 7.20 (1H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 162.6, 162.3, 150.7, 150.2, 139.4, 135.4, 130.7, 129.1, 129.0, 127.4, 125.1, 123.3, 118.3, 117.8, 114.9, 111.1, 104.8; IR (KBr) 3422, 3036, 2367, 1684, 1620, 1276, 1083, 757 cm<sup>-1</sup>; HRMS *m/z* (M<sup>+</sup>) calcd for C<sub>19</sub>H<sub>12</sub>O<sub>3</sub>: 288.0786. Found: 288.0788.

7-Hydroxy-8-methyl-9-phenyl-6*H*-benzo[*c*]chromen-6-one (17). Reaction of **1a** (224 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded **17** (154 mg, 51%) as a solid: mp 166–168 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.76 (1H, s), 7.99 (1H, d, *J* = 8.1 Hz), 7.51–7.28 (9H, m), 2.25 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 160.7, 151.0, 150.4, 140.6, 131.6, 130.3, 128.7, 128.3, 127.8, 124.9, 123.9, 122.9, 118.4, 117.5, 113.3, 104.1, 13.0; IR (KBr) 3449,

123.9, 122.9, 118.4, 117.5, 113.3, 104.1, 13.0; IR (KBr) 3449, 3062, 2370, 1677, 1268, 1125, 754 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>20</sub>H<sub>14</sub>O<sub>3</sub>: 302.0943. Found: 302.0943.

7-Hydroxy-8,9-diphenyl-6*H*-benzo[*c*]chromen-6-one (18). 1 Reaction of 1a (224 mg, 1.0 mmol) and β-ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 18 (211 mg, 58%) as a solid: mp 213–215 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.77 (1H, s), 8.00 (1H, d, *J* = 7.5 Hz), 7.60 (1H, s), 5 7.47–7.31 (3H, m), 7.21–7.19 (6H, m), 7.16–7.13 (4H, m); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 160.0, 150.5, 150.3, 140.2, 134.8, 133.6, 131.0, 130.5, 129.4, 128.4, 127.9, 127.7, 127.5, 127.1, 125.1, 123.1, 118.1, 117.6, 114.0, 104.8; IR (KBr) 3448, 3063, 1674, 1612, 1396, 1265, 1127, 752, 697 cm<sup>-1</sup>; HRMS *m/z* (M<sup>+</sup>) calcd for C<sub>25</sub>H<sub>16</sub>O<sub>3</sub>: 364.1099. Found: 364.1098.

Ethyl-7-hydroxy-6-oxo-9-phenyl-6*H*-benzo[*c*]chromene-8-carboxylate (19). Reaction of 1a (224 mg, 1.0 mmol) and β-ketoester 2d (303 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 19 (216 mg, 60%) as a solid: mp 193–195 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.67 (1H, s), 7.84 (1H, d, *J* = 7.5 Hz), 7.36–7.35 (7H, m), 7.24–7.17 (2H, m), 4.07 (2H, q, *J* = 7.2 Hz), 0.938 (3H, t, *J* = 7.2 Hz); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.9, 164.7, 159.5, 150.5, 148.9, 139.0, 135.5, 131.2, 128.6, 128.4, 127.8, 125.2, 123.2, 121.4, 117.5, 117.2, 113.1, 104.3, 61.3, 13.5; IR (KBr) 3455, 3106, 1737, 1552, 1127, 1015, 858, 742 cm<sup>-1</sup>; HRMS *m*/*z* (M<sup>+</sup>) calcd for C<sub>22</sub>H<sub>16</sub>O<sub>5</sub>: 360.0998. Found: 360.0994.

**7-Hydroxy-8,10-dimethyl-9-phenyl-6***H***-benzo[***c***]chromen-6-one (20). Reaction of <b>1b** (238 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded **20** (158 mg, 50%) as a solid: mp 207–209 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  12.07 (1H, s), 8.18 (1H, d, *J* = 8.1 Hz), 7.50–7.37 (5H, m), 7.29 (1H, t, *J* = 7.2 Hz), 7.14 (2H, d, *J* = 7.2 Hz), 2.36 (3H, s), 1.98 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  166.4, 158.9, 153.1, 150.4, 140.6, 129.2, 128.8, 128.3, 127.8, 127.8, 127.4, 125.1, 124.1, 123.3, 120.2, 117.5, 105.3, 22.0, 13.9; IR (KBr) 3437, 3067, 1685, 1616, 1272, 1124, 758 cm<sup>-1</sup>; HRMS *m/z* (M<sup>+</sup>) calcd for C<sub>21</sub>H<sub>16</sub>O<sub>3</sub>: 316.1099. Found: 316.1099.

**7-Hydroxy-2-methyl-9-phenyl-6H-benzo**[*c*]**chromen-6-one** (21). Reaction of **1c** (238 mg, 1.0 mmol) and β-ketoester **2a** (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded **21** (211 mg, 70%) as a solid: mp 198–200 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.27 (1H, s), 7.66 (1H, s), 7.57–7.54 (3H, m), 7.42–7.34 (3H, m), 7.15–7.06 (3H, m), 2.33 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.3, 162.5, 149.9, 148.7, 139.4, 135.3, 134.7, 131.5, 128.9, 128.9, 127.3, 123.0, 117.7, 117.3, 114.6, 110.7, 104.7, 21.0; IR (KBr) 3434, 3033, 1680, 1560, 1227, 1211, 45 1096, 758, 696 cm<sup>-1</sup>; HRMS *m/z* (M<sup>+</sup>) calcd for C<sub>20</sub>H<sub>14</sub>O<sub>3</sub>: 302.0943. Found: 302.0945.

**7-Hydroxy-2,8-dimethyl-9-phenyl-6***H***-benzo[***c***]chromen-6-one (22). Reaction of 1c (238 mg, 1.0 mmol) and β-ketoester 2b (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) 50 afforded 22 (164 mg, 52%) as a solid: mp 193–195 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) \delta 11.66 (1H, s), 7.61 (1H, s), 7.41–7.33 (3H, m), 7.31–7.26 (3H, m), 7.10–7.06 (2H, m), 2.29 (3H, s), 2.11 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) \delta 165.7, 160.7, 150.8, 148.4, 140.6, 134.6, 131.6, 130.9, 128.7, 128.3, 127.8, 123.6, 122.8, 55 117.9, 117.1, 113.1, 104.1, 21.0, 13.0; IR (KBr) 3456, 2932, 1688, 1602, 1513, 1375, 1190, 1014, 821, 745 cm<sup>-1</sup>; HRMS** *m/z* **(M<sup>+</sup>) calcd for C<sub>21</sub>H<sub>16</sub>O<sub>3</sub>: 316.1099. Found: 316.1097.** 

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2-Bromo-7-hydroxy-8-methyl-9-phenyl-6*H*-benzo[*c*]chromen-6-one (23). Reaction of 1d (301 mg, 1.0 mmol) and  $\beta$ -ketoester **2b** (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 23 (209 mg, 55%) as a solid: mp 216-218 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.59 (1H, s), 8.02 (1H, s), 7.50-7.39 (4H, m), 7.36–7.32 (3H, m), 7.17 (1H, d, I = 8.7 Hz), 2.20 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 165.1, 160.8, 151.2, 149.2, 140.3, 132.8, 130.2, 128.7, 128.4, 128.0, 125.7, 125.0, 120.2, 119.2, 118.0, 113.5, 103.9, 13.1; IR (KBr) 3449, 3064, 1703, 1625, 1557, 1409, 1264, 1217, 1082, 853, 691 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>20</sub>H<sub>13</sub>BrO<sub>3</sub>: 380.0048. Found: 380.0050.

2-Bromo-7-hydroxy-8,9-diphenyl-6*H*-benzo[*c*]chromen-6-one (24). Reaction of 1d (301 mg, 1.0 mmol) and β-ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) 15 afforded 24 (243 mg, 63%) as a solid: mp 215–217 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.67 (1H, s), 8.12 (1H, s), 7.55-7.53 (2H, m), 7.22-7.19 (7H, m), 7.14-7.09 (4H, m); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) & 165.1, 160.2, 150.7, 149.5, 140.0, 134.6, 133.3, 132.3,

130.9, 129.4, 129.3, 128.0, 127.8, 127.6, 127.2, 126.0, 120.0, 20 119.4, 118.2, 114.2, 104.7; IR (KBr) 3454, 3064, 1681, 1612, 1545, 1393, 1260, 1203, 1115, 880, 743, 701 cm<sup>-1</sup>; HRMS m/z $(M^{+})$  calcd for C<sub>25</sub>H<sub>15</sub>BrO<sub>3</sub>: 442.0205. Found: 442.0202.

7-Hydroxy-2-methyl-9-*p*-tolyl-6*H*-benzo[*c*]chromen-6-one (25). 25 Reaction of 1e (252 mg, 1.0 mmol) and  $\beta$ -ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 25 (221 mg, 70%) as a solid: mp 258–260 °C; <sup>1</sup>H NMR (300 MHz,  $CDCl_3 \delta$  11.40 (1H, s), 7.85 (1H, s), 7.72 (1H, s), 7.58 (2H, d, J = 7.5 Hz), 7.31–7.24 (5H, m), 2.45 (3H, s), 2.42 (3H, s); <sup>13</sup>C NMR

30 (75 MHz, CDCl<sub>3</sub>) δ 165.7, 160.7, 151.0, 150.4, 137.7, 137.7, 131.6, 129.9, 129.0, 128.7, 124.9, 123.9, 122.9, 118.5, 117.5, 113.4, 104.0, 21.2, 13.1; IR (KBr) 3434, 2928, 1690, 1618, 1588, 1437, 1240, 1181, 1076, 926, 784 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>21</sub>H<sub>16</sub>O<sub>3</sub>: 316.1099. Found: 316.1102.

35 7-Hydroxy-2,8-dimethyl-9-*p*-tolyl-6*H*-benzo[*c*]chromen-6-one (26). Reaction of 1e (252 mg, 1.0 mmol) and  $\beta$ -ketoester 2b (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 26 (178 mg, 54%) as a solid: mp 190–192 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.64 (1H, s), 7.59 (1H, s), 7.2 (1H, s), 40 7.21-7.15 (4H, m), 7.11-7.04 (2H, m), 2.35 (3H, s), 2.28 (3H, s), 2.11 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.7, 160.6, 150.8, 148.4, 137.7, 137.6, 134.5, 131.5, 130.8, 128.9, 128.6, 123.6, 122.8, 117.9, 117.1, 113.2, 103.9, 21.2, 21.0, 13.0; IR (KBr)  $3442, 3056, 1672, 1610, 1398, 1270, 1136, 1019, 862, 761 \text{ cm}^{-1};$ 45

HRMS m/z (M<sup>+</sup>) calcd for C<sub>22</sub>H<sub>18</sub>O<sub>3</sub>: 330.1256. Found: 330.1256. Ethyl 7-hydroxy-2-methyl-6-oxo-9-p-tolyl-6H-benzo[c]chro-

mene-8-carboxylate (27). Reaction of 1e (252 mg, 1.0 mmol) 50 and  $\beta$ -ketoester 2d (303 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 27 (240 mg, 62%) as a solid: mp 223–225 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.78 (1H, s), 7.73 (1H, s), 7.46 (1H, s), 7.32–7.17 (6H, m), 4.12 (2H, q, J = 7.2 Hz), 2.37 (3H, s), 2.34 (3H, s), 1.01 (3H, t, J = 7.2 Hz); <sup>13</sup>C NMR 55 (75 MHz, CDCl<sub>3</sub>) δ 166.3, 165.2, 159.8, 149.1, 149.0, 138.7, 136.4, 135.8, 135.0, 132.2, 129.2, 128.0, 123.4, 121.6, 117.5, 117.3, 113.3, 104.8, 61.5, 21.2, 21.0, 13.7; IR (KBr) 3438, 2989, 2733, 1732, 1671, 1552, 1405, 1248, 1205, 1133, 1021,

824 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>24</sub>H<sub>20</sub>O<sub>5</sub>: 388.1311. 1 Found: 388.1313.

7-Hydroxy-3-methoxy-9-(3-methoxyphenyl)-6*H*-benzo[*c*]chromen-6-one (28). Reaction of 1f (284 mg, 1.0 mmol) and  $\beta$ -ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 5 2.0 mmol) afforded 28 (250 mg, 72%) as a solid: mp 190-192 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.26 (1H, s), 7.92 (1H, d, J = 8.7 Hz), 7.57 (1H, s), 7.35 (1H, t, J = 7.8 Hz),7.20-7.18 (2H, m), 7.13-7.12 (1H, m), 6.94-6.80 (3H, m), 3.82 10(6H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 165.8, 162.1, 160.5, 159.4, 151.6, 150.9, 142.1, 132.1, 129.3, 123.9, 122.5, 121.1, 114.5, 113.1, 112.8, 112.5, 111.4, 103.3, 101.4, 55.6, 55.3; IR (KBr) 3449, 2930, 1679, 1632, 1623, 1464, 1396, 1266, 1092, 1029, 800, 725 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>21</sub>H<sub>16</sub>O<sub>5</sub>: 348.0998. 15 Found: 348.0999.

7-Hydroxy-3-methoxy-9-(3-methoxyphenyl)-8-methyl-6H-benzo-[c]chromen-6-one (29). Reaction of 1f (284 mg, 1.0 mmol) and  $\beta$ -ketoester 2b (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 29 (153 mg, 54%) as a solid: mp 20 171–173 °C; <sup>1</sup>H NMR (300 MHz,  $CDCl_3$ )  $\delta$  11.57 (1H, s), 7.75 (1H, d, J = 8.7 Hz), 7.32–7.24 (2H, m), 6.89–6.72 (5H, m), 3.78 (3H, s), 3.77 (3H, s), 2.11 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.9, 161.1, 160.6, 159.4, 151.6, 150.9, 142.1, 132.1, 129.3, 123.9, 122.5, 121.1, 114.5, 113.1, 112.8, 112.5, 111.4, 103.3, 25101.4, 55.6, 55.3, 12.9; IR (KBr) 3448, 2929, 1672, 1622, 1482, 1282, 1137, 1033, 798, 751 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>22</sub>H<sub>18</sub>O<sub>5</sub>: 362.1154. Found: 362.1154.

7-Hydroxy-3-methoxy-9-(3-methoxyphenyl)-8-phenyl-6H-benzo-[c]chromen-6-one (30). Reaction of 1f (284 mg, 1.0 mmol) and 30 β-ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 30 (254 mg, 60%) as a solid: mp 216–218 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.69 (1H, s), 7.87 (1H, d, J = 9.0 Hz), 7.47 (1H, s), 7.24-7.06 (6H, m), 6.88-6.80 (2H, m), 6.73-6.88 (2H, m), 6.56 (1H, s) 3.82 (3H, s), 3.52 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.8, 161.7, 161.6, 160.0, 158.9, 151.9, 150.2, 141.6, 135.0, 134.2, 130.9, 129.0, 127.8, 127.1, 124.2, 121.8, 114.8, 113.5, 113.1, 111.1, 104.0, 101.4, 55.7, 55.1; IR (KBr) 3444, 2935, 1679, 1639, 1464, 1396, 1266, 40 1092, 1029, 805, 735 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>27</sub>H<sub>20</sub>O<sub>5</sub>: 424.1311. Found: 424.1309.

7-Hydroxy-9-*p*-tolyl-6*H*-benzo[*c*]chromen-6-one (31). Reaction of 1g (238 mg, 1.0 mmol) and  $\beta$ -ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 31 45 (208 mg, 69%) as a solid: mp 199-201 °C; <sup>1</sup>H NMR (300 MHz,  $CDCl_3$ )  $\delta$  11.34 (1H, s), 8.07 (2H, d, J = 7.2 Hz), 7.73 (1H, s), 7.50-7.45 (1H, m), 7.37-7.25 (5H, m), 2.41 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 165.3, 162.5, 150.7, 150.2, 139.1, 136.5, 135.3, 130.6, 129.7, 127.2, 125.0, 123.3, 118.4, 117.7, 114.6, 50 110.8, 104, 12.2; IR (KBr) 3436, 3128, 1686, 1623, 1273, 1110, 944, 813, 752, 705 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>20</sub>H<sub>14</sub>O<sub>3</sub>: 302.0943. Found: 302.0946.

7-Hydroxy-9-(4-methoxyphenyl)-8-methyl-6H-benzo[c]chromen-55 6-one (32). Reaction of 1h (254 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 32 (182 mg, 55%) as a solid: mp 192–194 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.62 (1H, s), 7.87 (1H, d, J = 7.8 Hz)),

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7.36-7.31 (2H, m), 7.24-7.17 (4H, m), 6.92 (2H, d, *J* = 8.4 Hz), 3.80 (3H, s), 2.14 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.6, 160.7, 159.3, 150.6, 150.3, 132.8, 131.5, 130.0, 129.9, 124.9, 123.9, 122.9, 118.4, 117.5, 113.7, 113.4, 103.8, 55.3, 13.1; IR (KBr) 3453, 3073, 1675, 1612, 1510, 1274, 1129, 1029, 834, 736 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>21</sub>H<sub>16</sub>O<sub>4</sub>: 332.1049. Found: 332.1050.

7-Hydroxy-9-(pyridin-3-yl)-6*H*-benzo[*c*]chromen-6-one (33). Reaction of 1i (225 mg, 1.0 mmol) and  $\beta$ -ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 33 (220 mg, 70%) as a solid: mp 243–245 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.41 (1H, s), 8.93 (1H, s), 8.69 (1H, s), 8.07 (1H, d, J = 8.1 Hz), 7.97 (1H, d, J = 7.5 Hz), 7.72 (1H, s), 7.52–7.36 (4H, m), 7.22 (1H, s);  ${}^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  164.6, 162.6, 150.5, 149.5, 149.5, 139.0, 133.9, 133.4, 129.2, 129.1, 127.3, 126.0, 120.1, 119.4, 118.1, 115.6, 111.1, 104.6; IR (KBr) 3425, 3043, 1685, 1621, 1276, 1207, 1086, 754, 707 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>)

calcd for C<sub>18</sub>H<sub>11</sub>NO<sub>3</sub>: 289.0739. Found: 289.0741. 7-Hydroxy-8-phenyl-9-(pyridin-3-yl)-6H-benzo[c]chromen-6-20 one (34). Reaction of 1i (225 mg, 1.0 mmol) and  $\beta$ -ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 34 (229 mg, 63%) as a solid: mp 247–249 °C; <sup>1</sup>H NMR  $(300 \text{ MHz}, \text{CDCl}_3) \delta 11.82 (1\text{H}, \text{s}), 8.48 (2\text{H}, \text{d}, J = 7.8 \text{ Hz}), 8.03$ 25 (1H, d, J = 8.1 Hz), 7.59 (1H, s), 7.49 (1H, t, J = 6.9 Hz),7.40–7.35 (3H, m), 7.23–7.24 (3H, m), 7.14–7.12 (3H, m); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.4, 160.2, 150.6, 149.4, 148.3, 146.3, 137.0, 136.2, 134.1, 134.0, 131.0, 130.9, 128.7, 128.1, 127.5, 125.3, 123.1, 122.7, 117.8, 117.7, 113.6, 105.5; IR (KBr) 30 3443, 3056, 1663, 1610, 1391, 1264, 1129, 748 cm<sup>-1</sup>; HRMS m/z

 $(M^+)$  calcd for C<sub>24</sub>H<sub>15</sub>NO<sub>3</sub>: 365.1052. Found: 365.1049.

9-(2,5-Dimethylfuran-3-yl)-7-hydroxy-6H-benzo[c]chromen-6-one (35). Reaction of 1j (242 mg, 1.0 mmol) and β-ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 35 (217 mg, 71%) as a solid: mp 141–143 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.29 (1H, s), 7.95 (1H, d, J = 8.7 Hz), 7.47-7.41 (2H, m), 7.33-7.28 (2H, m), 7.00 (1H, s), 6.17 (1H, s), 2.47 (3H, s), 2.29 (3H, s);  $^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.1, 162.3, 150.6, 150.5, 148.1, 143.8, 135.0, 130.5, 124.9, 123.1, 120.5, 118.2, 117.7, 114.4, 110.7, 106.2, 103.7, 13.5, 13.3; IR (KBr) 3449, 2930, 1719, 1511, 1278, 1128, 817, 557 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>19</sub>H<sub>14</sub>O<sub>4</sub>: 306.0892. Found: 306.0890.

9-(2,5-Dimethylfuran-3-yl)-7-hydroxy-8-methyl-6*H*-benzo[*c*]-45 chromen-6-one (36). Reaction of 1j (242 mg, 1.0 mmol) and  $\beta$ -ketoester 2b (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 36 (169 mg, 53%) as a solid: mp 144–146 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.61 (1H, s), 7.89

50 (1H, d, J = 7.8 Hz), 7.39–7.34 (2H, m), 7.27–7.17 (2H, m), 5.93 (1H, s), 2.25 (3H, s), 2.16 (6H, s);  $^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$ 165.7, 160.7, 150.4, 150.0, 147.0, 143.8, 131.5, 130.0, 125.0, 124.9, 122.9, 120.6, 118.5, 117.6, 113.6, 108.1, 103.9, 13.4, 13.0, 12.5; IR (KBr) 3449, 3067, 1686, 1624, 1272, 1124, 757 cm<sup>-1</sup>; 55 HRMS m/z (M<sup>+</sup>) calcd for C<sub>20</sub>H<sub>16</sub>O<sub>4</sub>: 320.1049. Found: 320.1046.

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9-(2,5-Dimethylfuran-3-yl)-7-hydroxy-8-phenyl-6*H*-benzo[*c*]chromen-6-one (37). Reaction of 1j (242 mg, 1.0 mmol) and

 $\beta$ -ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 1 2.0 mmol) afforded 37 (248 mg, 65%) as a solid: mp 208-210 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.71 (1H, s), 7.96 (1H, d, J = 7.8 Hz), 7.49 (1H, s), 7.43 (1H, t, J = 7.8 Hz), 7.33-7.18 (7H, m), 5.51 (1H, s), 2.08 (3H, s), 1.92 (3H, s); <sup>13</sup>C 5 NMR (75 MHz, CDCl<sub>3</sub>) δ 165.6, 160.1, 150.6, 149.6, 147.2, 143.5, 135.1, 133.4, 130.6, 130.5, 127.8, 127.2, 125.1, 123.0, 120.6, 118.2, 117.7, 114.1, 108.2, 105.4, 104.5, 13.2, 12.5; IR (KBr) 3444, 3067, 1680, 1624, 1272, 1124, 759 cm<sup>-1</sup>; HRMS *m*/*z* 10(M<sup>+</sup>) calcd for C<sub>25</sub>H<sub>18</sub>O<sub>4</sub>: 382.1205. Found: 382.1208.

2-Bromo-9-(2,5-dimethylthiophen-3-yl)-7-hydroxy-6H-benzo[c]chromen-6-one (38). Reaction of 1k (337 mg, 1.0 mmol) and  $\beta$ -ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 38 (292 mg, 73%) as a solid: mp 15 217-219 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.16 (1H, s), 8.03 (1H, s), 7.49 (1H, d, J = 8.7 Hz), 7.39 (1H, s), 7.16 (1H, d, J = 8.7 Hz), 7.01 (1H, s), 6.70 (1H, s), 2.43 (3H, s), 2.39 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 164.6, 162.4, 149.6, 146.4, 136.7, 136.3, 134.6, 133.6, 133.4, 126.4, 126.0, 120.2, 119.5, 118.1, 20 116.9 112.6, 104.0, 15.0, 14.3; IR (KBr) 3451, 2377, 1677, 1390, 1268, 756 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>19</sub>H<sub>13</sub>BrO<sub>3</sub>S: 399.9769. Found: 399.9771.

2-Bromo-9-(2,5-dimethylthiophen-3-yl)-7-hydroxy-8-methyl-6H-benzo[c]chromen-6-one (39). Reaction of 1k (337 mg, 251.0 mmol) and  $\beta$ -ketoester 2b (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 39 (207 mg, 73%) as a solid: mp 213–215 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.63 (1H, s), 8.09 (1H, s), 7.54 (1H, d, J = 9.0 Hz), 7.36 (1H, s), 7.25 (1H, d, J = 8.7 Hz), 6.56 (1H, s), 2.50 (3H, s), 2.24 (3H, s), 2.19 (3H, 30 s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.2, 160.8, 149.3, 146.7, 136.7, 136.5, 133.4, 132.8, 130.1, 126.6, 126.2, 125.8, 120.3, 119.3, 118.0, 113.7, 104.0, 15.1, 13.6, 12.9; IR (KBr) 3477, 1689, 1551, 1388, 1259, 1122, 734 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for 35 C<sub>20</sub>H<sub>15</sub>BrO<sub>3</sub>S: 413.9925. Found: 413.9927.

Ethyl 2-bromo-9-(2,5-dimethylthiophen-3-yl)-7-hydroxy-6-oxo-6H-benzo[c]chromene-8-carboxylate (40). Reaction of 1k (337 mg, 1.0 mmol) and  $\beta$ -ketoester 2d (216 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 40 (207 mg, 64%) 40 as a solid: mp 203–205 °C; <sup>1</sup>H NMR (300 MHz,  $CDCl_3$ )  $\delta$  11.68 (1H, s), 8.1 (1H, s), 7.6 (1H, d, J = 7.6 Hz), 7.39 (1H, s), 7.26 (1H, d, J = 8.7 Hz), 6.57 (1H, s), 4.15 (2H, q, J = 7.2 Hz), 2.41 (3H, s), 2.29 (3H, s), 1.09 (3H, t, J = 7.2 Hz); <sup>13</sup>C NMR (75 MHz,  $CDCl_3$ )  $\delta$  165.6, 164.4, 159.7, 149.8, 145.3, 136.5, 135.0, 134.4, 45134.2, 134.1, 126.4, 126.3, 123.5, 119.6, 119.5, 118.4, 114.1, 104.9, 61.5, 15.0, 13.8, 13.7; IR (KBr) 3477, 1689, 1551, 1388, 1259, 1122, 734 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>22</sub>H<sub>17</sub>BrO<sub>5</sub>S: 471.9980. Found: 471.9982.

7-Hydroxy-9-(naphthalen-2-yl)-6*H*-benzo[*c*]chromen-6-one 50 (41). Reaction of 1l (274 mg, 1.0 mmol) and β-ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 41 (212 mg, 63%) as a solid: mp 228–230 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.40 (1H, s), 8.14 (2H, d, J = 6.9 Hz), 7.97-7.88 (4H, m), 7.78 (1H, d, J = 8.1 Hz), 7.55-7.48 (3H, m), 7.39–7.35 (3H, m); <sup>13</sup>C NMR (75 MHz,  $CDCl_3$ )  $\delta$  165.9, 161.8, 152.0, 150.8, 138.1, 133.1, 133.7, 131.7, 131.0, 128.2, 127.9, 127.8, 127.7, 126.7, 126.5, 126.4, 125.0, 124.5, 123.0, 118.4,

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117.9, 113.5, 104.8; IR (KBr) 3422, 2370, 1683, 1620, 1557, 1272, 1081, 858, 755 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>23</sub>H<sub>14</sub>O<sub>3</sub>: 338.0943. Found: 338.0943.

7-Hydroxy-8-methyl-9-(naphthalen-2-yl)-6*H*-benzo[*c*]chromen-5 6-one (42). Reaction of 1l (274 mg, 1.0 mmol) and  $\beta$ -ketoester 2b (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 42 (179 mg, 51%) as a solid: mp 194–196 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 11.68 (1H, s), 7.90-7.79 (4H, m), 7.74 (1H, s), 7.47-7.44 (3H, m), 7.41-7.33 (2H, m), 7.27-7.16 (2H, m), 10 2.17 (3H, s);  ${}^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.7, 160.8, 151.0, 150.5, 138.1, 133.1, 132.7, 131.7, 130.0, 128.12, 127.9, 127.8, 127.7, 126.7, 126.5, 126.4, 125.0, 124.1, 123.0, 118.4, 117.6, 113.5, 104.3, 13.2; IR (KBr) 3447, 3053, 1676, 1268, 1123, 755 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>24</sub>H<sub>16</sub>O<sub>3</sub>: 352.1099. 15 Found: 352.1097.

7-Hydroxy-9-(naphthalen-2-yl)-8-phenyl-6H-benzo[c]chromen-6-one (43). Reaction of 1l (274 mg, 1.0 mmol) and  $\beta$ -ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 43 (207 mg, 50%) as a solid: mp 199–201 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.84 (1H, s), 8.09 (1H, d, J = 7.2 Hz), 7.76–7.47 (4H, m), 7.6 (1H, d, J = 8.4 Hz), 7.53–7.33 (5H, m), 7.22-7.18 (5H, m), 7.15-7.12 (1H, m); <sup>13</sup>C NMR (75 MHz,  $CDCl_3$ )  $\delta$  165.9, 160.4, 150.9, 150.4, 138.2, 135.0, 134.0, 133.2, 132.5, 131.2, 130.9, 128.8, 128.3, 128.1, 127.8, 127.5, 127.5, 127.4, 126.6, 126.5, 125.4, 123.4, 118.4, 117.9, 114.6, 105.2; IR (KBr) 3424, 3055, 1672, 1612, 1265, 857, 748 cm<sup>-1</sup>; HRMS m/z $(M^{+})$  calcd for C<sub>29</sub>H<sub>18</sub>O<sub>3</sub>: 414.1256. Found: 414.1254.

- 9-Cyclopropyl-7-hydroxy-6H-benzo[c]chromen-6-one (44). 30 Reaction of 1m (188 mg, 1.0 mmol) and β-ketoester 2a (195 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 44 (181 mg, 72%) as a solid: mp 140-142 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.19 (1H, s), 7.91 (1H, d, J = 7.5 Hz), 7.42-7.37 (1H, m), 7.28-7.19 (3H, m), 6.59 (1H, s), 1.95-1.89
- 35 (1H, m), 1.12–1.04 (2H, m), 0.85–0.78 (2H, m); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.1, 162.4, 155.5, 150.6, 134.7, 130.3, 124.8, 123.1, 118.2, 117.6, 112.4, 109.8, 103.6, 16.5, 10.7; IR (KBr) 3394, 3069, 1663, 1563, 1422, 1333, 1276, 1207, 1080, 986, 759 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>16</sub>H<sub>12</sub>O<sub>3</sub>: 252.0786. 40Found: 252.0785.

9-Cyclopropyl-7-hydroxy-8-phenyl-6*H*-benzo[*c*]chromen-6-one (45). Reaction of 1m (188 mg, 1.0 mmol) and  $\beta$ -ketoester 2c (288 mg, 1.5 mmol) using Cs<sub>2</sub>CO<sub>3</sub> (650 mg, 2.0 mmol) afforded 45 (200 mg, 61%) as a solid: mp 187–190 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  11.60 (1H, s), 7.99 (1H, d, J = 7.2 Hz), 7.51-7.31 (8H, m), 7.03 (1H, s), 1.83-1.76 (1H, m), 1.00-0.92 (2H, m), 0.90–0.84 (2H, m);  $^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  165.5, 159.4, 152.8, 150.6, 135.3, 133.8, 130.3, 130.0, 128.3, 127.5, 124.9, 122.9, 118.3, 117.6, 106.2, 103.5, 14.6, 10.9; IR (KBr) 3449, 3048, 1661, 1614, 1548, 1405, 1273, 1163, 760 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>22</sub>H<sub>16</sub>O<sub>3</sub>: 328.1099. Found: 328.1100.

#### General procedure for the synthesis of terphenyls (49-54) 55

To a solution of KOH (2.0 mmol) in DMSO (3.5 mL) and water (0.5 mL), CH<sub>3</sub>I (2.0 mmol) and benzo[c]chromen-6-ones (0.4 mmol) were added and the reaction mixture was stirred at room temperature for 1-2 h (progress of reaction was moni-1 tored by thin layer chromatography). The reaction mixture was extracted with ethyl acetate and evaporated in a rotary evaporator under reduced pressure. The residue was purified by flash column chromatography on silica gel to give the products. 5 Characterization data for all synthesized terphenyls 49-54 are as follows.

Methyl 2",5'-dimethoxy-2',6'-dimethyl-[1,1':3',1"-terphenyl]-4'-carboxylate (49). Reaction of 20 (126 mg, 0.4 mmol) and 10methyl iodide (284 mg, 2.0 mmol) using KOH (112 mg, 2.0 mmol) afforded 49 (105 mg, 70%) as a solid: mp 99-101 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.45-7.39 (2H, m), 7.35-7.26 (2H, m), 7.20-7.17 (1H, m), 7.13-7.09 (2H, m), 6.96-6.90 (2H, m), 3.82 (3H, s), 3.76 (3H, s), 3.48 (3H, s), 1.97 15 (3H, s), 1.66 (3H, s);  ${}^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  168.4, 156.9, 152.7, 144.6, 140.9, 134.6, 132.2, 131.2, 130.8, 128.9, 128.4, 128.1, 128.0, 126.8, 126.3, 120.2, 110.6, 62.1, 56.3, 51.6, 17.9, 14.0; IR (KBr) 3048, 1680, 1612, 1548, 1405, 1273, 1163, 768 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>24</sub>H<sub>24</sub>O<sub>4</sub>: 376.1675. 20 Found: 376.1677.

Methyl 5"-bromo-2",5'-dimethoxy-6'-methyl-[1,1':3',1"-terphenyl]-4'-carboxylate (50). Reaction of 23 (152 mg, 0.4 mmol) and methyl iodide (284 mg, 2.0 mmol) using KOH (112 mg, 2.0 mmol) afforded 50 (149 mg, 85%) as a solid: mp 83-85 °C; 25<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.43–7.30 (7H, m), 7.00 (1H, s), 6.78-6.74 (1H, m), 3.87 (3H, s), 3.72 (3H, s), 3.67 (3H, s), 2.23 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 167.7, 156.2, 155.3, 145.3, 140.6, 134.0, 133.1, 131.4, 131.0, 129.2, 129.0, 128.1, 127.6, 127.2, 126.6, 112.6, 112.0, 61.8, 55.5, 51.7, 13.6; IR (KBr) 3018, 30 1712, 1614, 1548, 1405, 1273, 1163, 749 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>23</sub>H<sub>21</sub>BrO<sub>4</sub>: 440.0623. Found: 440.0622.

Methyl 5'-(2,4-dimethoxyphenyl)-3,3'-dimethoxy-[1,1':2',1"terphenyl]-4'-carboxylate (51). Reaction of 30 (169 mg, 0.4 mmol) and methyl iodide (284 mg, 2.0 mmol) using KOH (112 mg, 2.0 mmol) afforded 51 (164 mg, 85%) as a solid: mp 68-70 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.27-7.24 (7H, m), 7.09 (1H, t, J = 8.1 Hz), 6.72-7.8 (2H, d, J = 7.8 Hz), 6.57-6.54 (3H, J = 7.8 Hz), 6m), 3.86 (3H, s), 3.79 (3H, s), 3.70 (3H, s), 3.57 (3H, s), 3.38 40 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  168.1, 160.7, 158.8, 157.2, 155.2, 143.5, 141.8, 137.0, 136.0, 132.9, 131.2, 130.9, 128.7, 128.6, 127.8, 127.7, 126.7, 122.2, 121.4, 114.9, 113.0, 104.3, 98.4, 61.5, 55.3, 55.0, 51.8; IR (KBr) 2935, 1731, 1608, 1458, 1282, 1159, 1039, 703 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for 45C<sub>30</sub>H<sub>28</sub>O<sub>6</sub>: 484.1886. Found: 384.1886.

5'-bromo-5-(2,5-dimethylthiophen-3-yl)-2',3-Methyl dimethoxy-[1,1'-biphenyl]-2-carboxylate (52). Reaction of 39 (104 mg, 0.4 mmol) and methyl iodide (284 mg, 2.0 mmol) using KOH (112 mg, 2.0 mmol) afforded 52 (141 mg, 80%) as a 50 solid: mp 140-142 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.40-7.35 (2H, m), 6.91 (1H, s), 6.89 (1H, s), 6.77 (1H, d, J = 8.7 Hz), 6.70 (1H, s), 3.88 (3H, s), 3.71 (3H, s), 3.62 (3H, s), 2.44 (3H, s), 2.42 (3H, s); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  167.5, 156.7, 155.3, 139.4, 137.2, 137.0, 136.0, 133.0, 132.7, 131.5, 131.1, 126.8, 123.2, 121.1, 112.5, 112.1, 110.7, 56.0, 55.5, 51.7, 15.0, 14.0; IR (KBr) 2939, 2369, 1733, 1599, 1443, 1251, 1108, 1072, 756, 704 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>22</sub>H<sub>21</sub>BrO<sub>4</sub>S: 460.0344. Found: 460.0342.

Methyl 2',3-dimethoxy-4-methyl-5-(naphthalen-2-yl)-[1,1'biphenyl]-2-carboxylate (53). Reaction of 29 (140 mg, 0.4 mmol) and methyl iodide (284 mg, 2.0 mmol) using KOH (112 mg, 2.0 mmol) afforded 53 (128 mg, 78%) as a solid: mp 113-115 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.81-7.78 (3H, m), 7.72 (1H, s), 7.42-7.39 (3H, m), 7.25-7.17 (2H, m), 7.07 (1H, s), 6.92-6.82 (2H, m), 3.83 (3H, s), 3.69 (3H, s), 3.57 (3H, s), 2.2 (3H, s);  ${}^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  167.8, 156.0, 155.5, 144.7, 138.2, 135.3, 132.9, 132.2, 130.5, 128.8, 128.7, 128.5, 127.9,

- 10 127.8, 127.7, 127.4, 127.3, 127.2, 126.8, 126.0, 125.8, 120.3, 110.3, 61.6, 55.1, 51.5, 13.5; IR (KBr) 3067, 1688, 1618, 1272, 1124, 751 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>27</sub>H<sub>24</sub>O<sub>4</sub>: 412.1675. Found: 412.1676.
- Methyl 5'-cyclopropyl-2,3'-dimethoxy-[1,1':4',1"-terphenyl]-2'-15 carboxylate (54). Reaction of 45 (131 mg, 0.4 mmol) and methyl iodide (284 mg, 2.0 mmol) using KOH (112 mg, 2.0 mmol) afforded 54 (133 mg, 86%) as a solid: mp 85-87 °C; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.39–7.18 (7H, m), 6.94 (1H, d, J =
- 7.5 Hz), 6.87 (1H, d, *I* = 8.4 Hz), 6.61 (1H, s), 3.71 (3H, s), 3.54 20 (3H, s), 3.32 (1H, s), 1.68–1.59 (1H, m), 0.74–0.61 (4H, m); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>) δ 167.9, 156.1, 154.9, 144.9, 137.4, 136.3, 135.0, 130.6, 130.5, 129.2, 129.0, 127.9, 127.0, 125.5, 121.5, 120.5, 110.5, 61.6, 55.3, 51.6, 13.5, 9.8; IR (KBr) 3009, 25 2942, 2842, 1731, 1604, 1544, 1280, 1143, 1022, 757, 706 cm<sup>-1</sup>; HRMS m/z (M<sup>+</sup>) calcd for C<sub>25</sub>H<sub>24</sub>O<sub>4</sub>: 388.1675. Found: 388.1673.

Crystal refinement data for compound 26 30

 $C_{44}H_{36}O_6$ , M = 660.73, triclinic, space group  $P_{bca}$ , a = 10.8607 (14) Å, b = 10.8607(14) Å, c = 15.2714(19) Å, V = 1644.3(4) Å<sup>3</sup>, Z = 2, T = 200(2) K,  $\rho_{\text{calcd}} = 1.335 \text{ mg m}^{-3}$ ,  $2\theta_{\text{max.}} = 26.08$ , refinement of 459 parameters on 6463 independent reflections out of 10 459 collected reflections ( $R_{int} = 0.0454$ ) led to  $R_1 = 0.0642$  $[I > 2\sigma(I)]$ , w $R_2 = 0.2354$  (all data) and S = 1.030 with the largest difference peak and hole of 0.307 and -0.429 e Å<sup>-3</sup> respectively.

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### Notes and references

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