Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2014, **12**, 919

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

Tej Narayan Poudel and Yong Rok Lee*

Received 3rd September 2013,
Accepted 29th November 2013

DOI: 10.1039/c3ob41800f

www.rsc.org/obc

Novel and efficient one-pot syntheses of a variety of benzo[*c*]chromen-6-one derivatives were accomplished using Cs_2CO_3-promoted reactions between substituted 2-hydroxychalcones and β-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.

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.[1] 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).[3] Some of these molecules exhibit biologically and pharmacologically important antitumor and antibiotic activities,[4] promote endothelial cell proliferation, and inhibit oestrogen receptor growth activities.[5] Benzo[*c*]chromen-6-ones have also been used as intermediates for the synthesis of pharmaceutically valuable compounds, such as progesterone, androgen, and glucocorticoid receptor agonists.[6] 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.[7] In addition, benzo[*c*]chromen-6-one derivatives are present in many foods, such as citrus fruits, herbs, and vegetables.[8] For example, autumnariol (**1**) was isolated from the bulbs of *Eucomis autumnalis* Gerab. (Liliaceae).[9a] Alternariol (**2**), another benzo[*c*]chromen-6-one derivative, is an important metabolite of toxin-producing *Alternaria* fungi, which causes significant crop losses by fouling of tomatoes, apples, and other fruits.[9b] Interestingly, alternariol (**2**) has been also shown to have antiviral, antimicrobial, anticancer, and cytotoxic activities.[9c–e] Palmariols A (**3**) and B (**4**) were isolated from discomycete *Lachnumpalmae* and exhibited antimicrobial, antinematodal, and acetylcholinesterase inhibitory activities.[9f,g] Graphislactones A (**5**) and B (**6**) were isolated

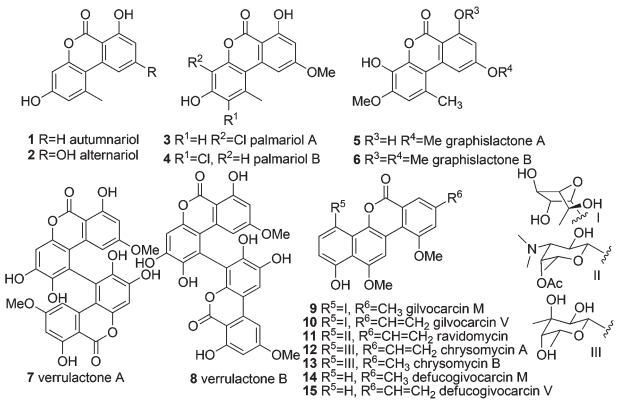


Fig. 1 Selected naturally occurring molecules bearing benzo[*c*]chromen-6-one moiety.

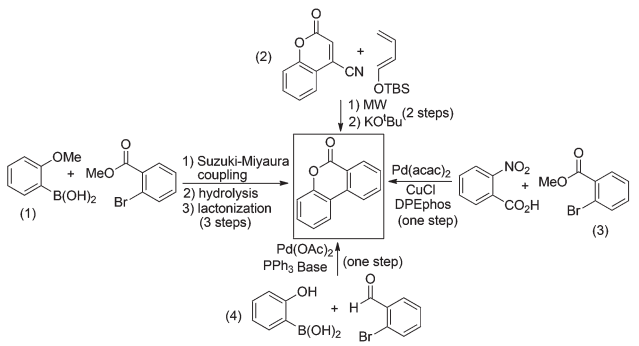
School of Chemical Engineering, Yeungnam University, Gyeongsan 712-749, Republic of Korea. E-mail: yrlee@yu.ac.kr; Fax: +82-53-810-4631; Tel: +82-53-810-2529

†Electronic supplementary information (ESI) available: Depiction of ^1H, ^{13}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 format see DOI: 10.1039/c3ob41800f

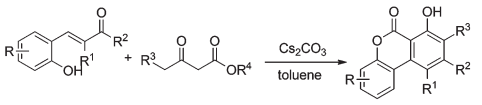
from the lichen *Graphisscripta* var. *pulverrulenta*.[10a–f] Graphislactone A (**5**) acts as an antioxidant and free radical scavenger,[11] and was found to be active against the SW1116 cell line and an active inhibitor of AChE.[10e] Verrulactones A (**7**) and B (**8**) were isolated from a culture broth of the fungal strain *Penicillium verruculosum* F375,[10a–f] and inhibited *Staphylococcus aureus* enoyl-ACP reductase with an IC_{50} of 0.92 μM and exhibited antibacterial activity against *S. aureus* and MRSA with MICs of 8 μg mL^{-1}.[12] 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.[13]

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 reaction followed by metal or Lewis acid-mediated lactonization of ester and methoxy groups (eqn (1), Scheme 1).[14] Recently, a new reaction involving a microwave-assisted Diels–Alder reaction between 4-cyanocoumarin and 1-oxygenated dienes followed by elimination and aromatization with a strong base was also described (eqn (2)).[15] 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 corresponding 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,[16] or by palladium acetate-catalyzed Suzuki–Miyaura coupling followed by oxidative lactonization (eqn (3) and (4)).[17] 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-6-one derivatives using inexpensive catalysts and reagents has yet 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



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



Scheme 2

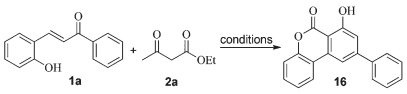
derivatives *via* domino Michael addition/intramolecular aldol/oxidative aromatization/lactonization reactions between substituted 2-hydroxychalcones and β-ketoesters.

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

Results and discussion

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 sodium methoxide in refluxing methanol for 12 h, **16** was produced in 40% yield. Using K_2CO_3 and Cs_2CO_3, 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 2 equivalents of Cs_2CO_3 afforded **16** in 71% yield. In recent years, Cs_2CO_3 has been widely used as an excellent base for a variety of transformations in organic synthesis.[18] Importantly, we found that Cs_2CO_3 is more efficient than other bases for the production of **16** in terms of yield and reaction time. 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 determined by analyzing spectral data. The ^{1}H NMR spectrum of **16** showed a single OH peak at δ 11.30 ppm in downfield due to hydrogen bonding with the ester carbonyl group, and

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



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
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

two single peaks at δ 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 ^{13}C NMR spectrum, which showed the expected carbonyl peak at δ 162.6 ppm due to the ester. In addition, the IR spectrum of **16** contained an ester carbonyl absorption at 1684 cm^{-1}.

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

Table 2 Additional reactions for the synthesis of a variety of benzo[*c*]chromen-6-one derivatives

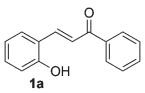
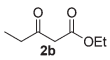
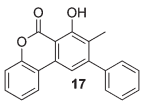
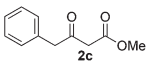
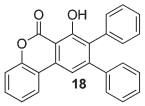
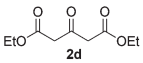
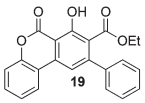
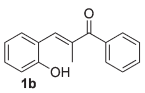
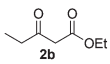
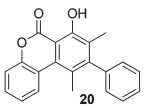
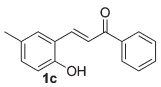
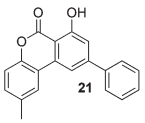
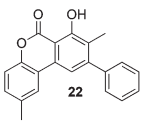
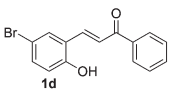
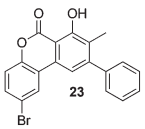
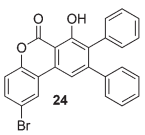
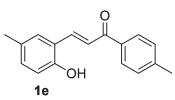
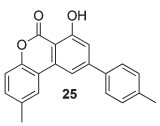
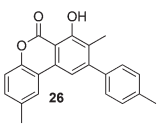
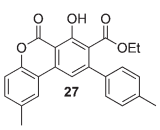
Entry	Chalcone	β-Ketoester	Time (h)	Product	Yield (%)
1			2		51
2	**1a**		2		58
3	**1a**		2		60
4			2		50
5		**2a**	2		70
6	**1c**	**2b**	2		52
7		**2a**	3		55
8	**1d**	**2c**	3		63
9		**2a**	2		70
10	**1e**	**2b**	3		54
11	**1e**	**2d**	3		62

Table 2 *(Contd.)*

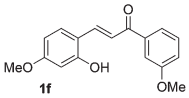
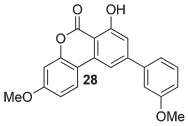
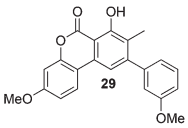
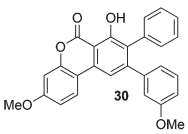
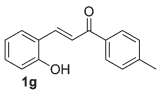
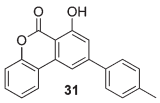
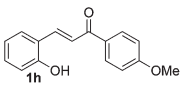
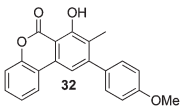
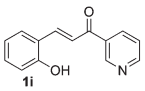
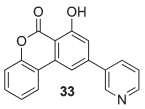
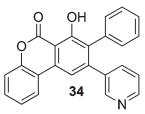
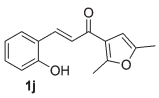
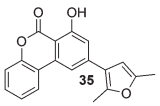
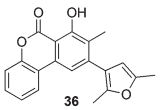
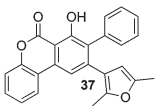
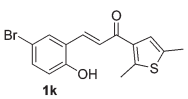
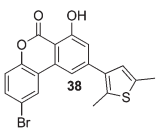
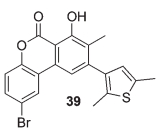
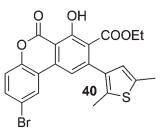
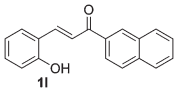
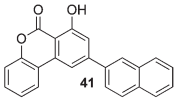
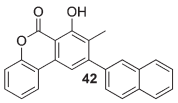
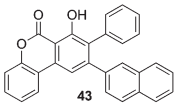
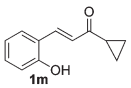
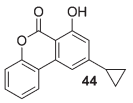
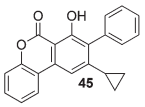
Entry	Chalcone	β-Ketoester	Time (h)	Product	Yield (%)
12		**2a**	2		72
13	**1f**	**2b**	2		54
14	**1f**	**2c**	3		60
15		**2a**	2		69
16		**2b**	2		55
17		**2a**	3		70
18	**1i**	**2c**	3		63
19		**2a**	3		71
20	**1j**	**2b**	3		53
21	**1j**	**2c**	3		65
22		**2a**	2		73
23	**1k**	**2b**	2		50
24	**1k**	**2d**	2		64

Table 2 *(Contd.)*

Entry	Chalcone	β-Ketoester	Time (h)	Product	Yield (%)
25	 1l	**2a**	2	 41	63
26	**1l**	**2b**	3	 42	51
27	**1l**	**2c**	3	 43	50
28	 1m	**2a**	2	 44	72
29	**1m**	**2c**	2	 45	61

oxopentanedioate (**2d**) in the presence of 2 equivalents of Cs_2CO_3 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** 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 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 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 (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-1-one (**1i**), (*E*)-3-(2-hydroxyphenyl)-1-(2,5-dimethylfuran-3-yl)-prop-2-en-1-one (**1j**), or (*E*)-3-(2-hydroxyphenyl)-1-(2,5-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-(naphthalene-2-yl)prop-2-en-1-one (**1l**) and β-ketoesters were also successful. When **1l** was treated with **2a**, **2b**, or **2c**, products **41–43** were produced in 63, 51, and 50% yield, respectively (entries 25–27). When (*E*)-1-cyclopropyl-3-(2-hydroxyphenyl)prop-2-en-1-one (**1m**) was used, compounds **44** 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 β-carbon to the carbonyl group of **1a** to give intermediate **46**, which undergoes an intramolecular aldol reaction followed by

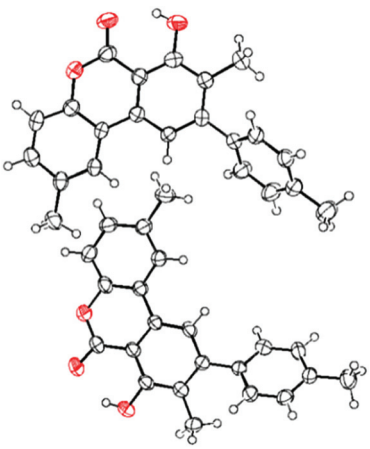
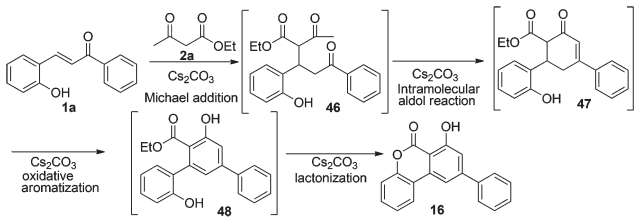


Fig. 2 X-ray structure of compound **26** containing two molecules in a unit.



Scheme 3 Proposed mechanism for the formation of 7-hydroxy-9-phenyl-6*H*-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 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[19] and exhibit a number of potent biological properties, which include antioxidant, neuroprotective, cytotoxic, antithrombotic, and anticoagulant activities.[20] In addition, these molecules play a significant role in the fields of optical materials, liquid crystals, spacers in catenane, and porphyrin chemistry.[21] Because of their important biological and physical properties, a number of synthetic methods have been devised to produce terphenyls.[22] These reactions typically included aryl zinc reagents with functionalized biphenyl nonaflates,[23] Grignard reagents containing dihalobenzenes, and triazene-substituted arylboronic esters.[24] Recently, other methodologies using Suzuki cross-coupling reactions between dihalobenzenes and arylboronic acids,[25] the gold-catalyzed cycloaromatization of dienynes,[26] DMEDA-catalyzed direct C–H arylation of unactivated benzenes,[27] and rhodium-catalyzed formal [2 + 2 + 2] cycloaddition reactions of alkynes have been described.[28] Although a number of methods have been reported for the synthesis of terphenyls, synthetic methods are still required for the production of polysubstituted terphenyls.

The conversions of several synthesized benzo[*c*]chromen-6-ones 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.

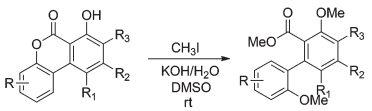
Conclusions

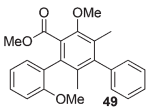
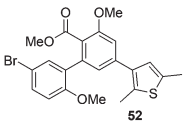
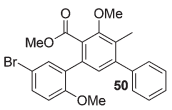
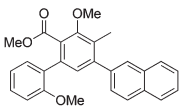
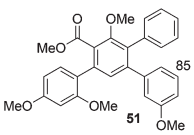
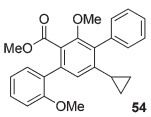
We described the Cs_2CO_3-promoted one-pot synthesis of biologically interesting benzo[*c*]chromen-6-one derivatives starting from substituted 2-hydroxychalcones and β-ketoesters. These reactions were accomplished by domino Michael addition/intramolecular aldol/oxidative aromatization/lactonization. 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. β-Ketoesters (**2a–d**) were purchased from Sigma-Aldrich. Merck precoated silica gel plates (Art. 5554) with a fluorescent indicator were used for analytical

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



Benzo[*c*]chromen-6-one	Time (h)	Product	Yield (%)	Benzo[*c*]chromen-6-one	Time (h)	Product	Yield (%)
20	2	 **49**	70	**39**	1	 **52**	87
23	1	 **50**	85	**42**	1	 **53**	78
30	2	 **51**	85	**42**	1	 **54**	86

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. ^{1}H NMR spectra were recorded on a Varian-VNS (300 MHz) spectrometer in $CDCl_3$ using 7.24 ppm as the solvent chemical shift. ^{13}C NMR spectra were recorded on a Varian-VNS (75 MHz) spectrometer in $CDCl_3$ 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 (1a–m)

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 × 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_2CO_3 (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_2CO_3 (650 mg, 2.0 mmol) afforded **16** (204 mg, 71%) as a solid: mp 213–215 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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^{-1}; HRMS m/z (M^+) calcd for $C_{19}H_{12}O_3$: 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_2CO_3 (650 mg, 2.0 mmol) afforded **17** (154 mg, 51%) as a solid: mp 166–168 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.76 (1H, s), 7.99 (1H, d, J = 8.1 Hz), 7.51–7.28 (9H, m), 2.25 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 3062, 2370, 1677, 1268, 1125, 754 cm^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{14}O_3$: 302.0943. Found: 302.0943.

7-Hydroxy-8,9-diphenyl-6*H*-benzo[*c*]chromen-6-one (18). Reaction of **1a** (224 mg, 1.0 mmol) and β-ketoester **2c** (288 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **18** (211 mg, 58%) as a solid: mp 213–215 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.77 (1H, s), 8.00 (1H, d, J = 7.5 Hz), 7.60 (1H, s), 7.47–7.31 (3H, m), 7.21–7.19 (6H, m), 7.16–7.13 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{25}H_{16}O_3$: 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_2CO_3 (650 mg, 2.0 mmol) afforded **19** (216 mg, 60%) as a solid: mp 193–195 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{22}H_{16}O_5$: 360.0998. Found: 360.0994.

7-Hydroxy-8,10-dimethyl-9-phenyl-6*H*-benzo[*c*]chromen-6-one (20). Reaction of **1b** (238 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **20** (158 mg, 50%) as a solid: mp 207–209 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{21}H_{16}O_3$: 316.1099. Found: 316.1099.

7-Hydroxy-2-methyl-9-phenyl-6*H*-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_2CO_3 (650 mg, 2.0 mmol) afforded **21** (211 mg, 70%) as a solid: mp 198–200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 1096, 758, 696 cm^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{14}O_3$: 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_2CO_3 (650 mg, 2.0 mmol) afforded **22** (164 mg, 52%) as a solid: mp 193–195 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 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^{-1}; HRMS m/z (M^+) calcd for $C_{21}H_{16}O_3$: 316.1099. Found: 316.1097.

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 β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **23** (209 mg, 55%) as a solid: mp 216–218 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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, J = 8.7 Hz), 2.20 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) 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^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{13}BrO_3$: 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_2CO_3 (650 mg, 2.0 mmol) afforded **24** (243 mg, 63%) as a solid: mp 215–217 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 119.4, 118.2, 114.2, 104.7; IR (KBr) 3454, 3064, 1681, 1612, 1545, 1393, 1260, 1203, 1115, 880, 743, 701 cm^{-1}; HRMS m/z (M^+) calcd for $C_{25}H_{15}BrO_3$: 442.0205. Found: 442.0202.

7-Hydroxy-2-methyl-9-*p*-tolyl-6*H*-benzo[*c*]chromen-6-one (25). Reaction of **1e** (252 mg, 1.0 mmol) and β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **25** (221 mg, 70%) as a solid: mp 258–260 °C; ^{1}H NMR (300 MHz, $CDCl_3$ δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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^{-1}; HRMS m/z (M^+) calcd for $C_{21}H_{16}O_3$: 316.1099. Found: 316.1102.

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 β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **26** (178 mg, 54%) as a solid: mp 190–192 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.64 (1H, s), 7.59 (1H, s), 7.2 (1H, s), 7.21–7.15 (4H, m), 7.11–7.04 (2H, m), 2.35 (3H, s), 2.28 (3H, s), 2.11 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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 cm^{-1}; HRMS m/z (M^+) calcd for $C_{22}H_{18}O_3$: 330.1256. Found: 330.1256.

Ethyl 7-hydroxy-2-methyl-6-oxo-9-*p*-tolyl-6*H*-benzo[*c*]chromene-8-carboxylate (27). Reaction of **1e** (252 mg, 1.0 mmol) and β-ketoester **2d** (303 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **27** (240 mg, 62%) as a solid: mp 223–225 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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^{-1}; HRMS m/z (M^+) calcd for $C_{24}H_{20}O_5$: 388.1311. 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 β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **28** (250 mg, 72%) as a solid: mp 190–192 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) 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^{-1}; HRMS m/z (M^+) calcd for $C_{21}H_{16}O_5$: 348.0998. Found: 348.0999.

7-Hydroxy-3-methoxy-9-(3-methoxyphenyl)-8-methyl-6*H*-benzo-[*c*]chromen-6-one (29). Reaction of **1f** (284 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **29** (153 mg, 54%) as a solid: mp 171–173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 101.4, 55.6, 55.3, 12.9; IR (KBr) 3448, 2929, 1672, 1622, 1482, 1282, 1137, 1033, 798, 751 cm^{-1}; HRMS m/z (M^+) calcd for $C_{22}H_{18}O_5$: 362.1154. Found: 362.1154.

7-Hydroxy-3-methoxy-9-(3-methoxyphenyl)-8-phenyl-6*H*-benzo-[*c*]chromen-6-one (30). Reaction of **1f** (284 mg, 1.0 mmol) and β-ketoester **2c** (288 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **30** (254 mg, 60%) as a solid: mp 216–218 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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, 1092, 1029, 805, 735 cm^{-1}; HRMS m/z (M^+) calcd for $C_{27}H_{20}O_5$: 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 β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **31** (208 mg, 69%) as a solid: mp 199–201 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.34 (1H, s), 8.07 (2H, d, J = 7.2 Hz), 7.73 (1H, s), 7.50–7.45 (2H, m), 7.37–7.25 (5H, m), 2.41 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) 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, 110.8, 104, 12.2; IR (KBr) 3436, 3128, 1686, 1623, 1273, 1110, 944, 813, 752, 705 cm^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{14}O_3$: 302.0943. Found: 302.0946.

7-Hydroxy-9-(4-methoxyphenyl)-8-methyl-6*H*-benzo[*c*]chromen-6-one (32). Reaction of **1h** (254 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **32** (182 mg, 55%) as a solid: mp 192–194 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.62 (1H, s), 7.87 (1H, d, J = 7.8 Hz)),

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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{21}H_{16}O_4$: 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 β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **33** (220 mg, 70%) as a solid: mp 243–245 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{18}H_{11}NO_3$: 289.0739. Found: 289.0741.

7-Hydroxy-8-phenyl-9-(pyridin-3-yl)-6*H*-benzo[*c*]chromen-6-one (34). Reaction of **1i** (225 mg, 1.0 mmol) and β-ketoester **2c** (288 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **34** (229 mg, 63%) as a solid: mp 247–249 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.82 (1H, s), 8.48 (2H, d, J = 7.8 Hz), 8.03 (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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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) 3443, 3056, 1663, 1610, 1391, 1264, 1129, 748 cm^{-1}; HRMS m/z (M^+) calcd for $C_{24}H_{15}NO_3$: 365.1052. Found: 365.1049.

9-(2,5-Dimethylfuran-3-yl)-7-hydroxy-6*H*-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_2CO_3 (650 mg, 2.0 mmol) afforded **35** (217 mg, 71%) as a solid: mp 141–143 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{19}H_{14}O_4$: 306.0892. Found: 306.0890.

9-(2,5-Dimethylfuran-3-yl)-7-hydroxy-8-methyl-6*H*-benzo[*c*]-chromen-6-one (36). Reaction of **1j** (242 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **36** (169 mg, 53%) as a solid: mp 144–146 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.61 (1H, s), 7.89 (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, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{16}O_4$: 320.1049. Found: 320.1046.

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 β-ketoester **2c** (288 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **37** (248 mg, 65%) as a solid: mp 208–210 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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^{-1}; HRMS m/z (M^+) calcd for $C_{25}H_{18}O_4$: 382.1205. Found: 382.1208.

2-Bromo-9-(2,5-dimethylthiophen-3-yl)-7-hydroxy-6*H*-benzo[*c*]-chromen-6-one (38). Reaction of **1k** (337 mg, 1.0 mmol) and β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **38** (292 mg, 73%) as a solid: mp 217–219 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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, 116.9 112.6, 104.0, 15.0, 14.3; IR (KBr) 3451, 2377, 1677, 1390, 1268, 756 cm^{-1}; HRMS m/z (M^+) calcd for $C_{19}H_{13}BrO_3S$: 399.9769. Found: 399.9771.

2-Bromo-9-(2,5-dimethylthiophen-3-yl)-7-hydroxy-8-methyl-6*H*-benzo[*c*]chromen-6-one (39). Reaction of **1k** (337 mg, 1.0 mmol) and β-ketoester **2b** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **39** (207 mg, 73%) as a solid: mp 213–215 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS m/z (M^+) calcd for $C_{20}H_{15}BrO_3S$: 413.9925. Found: 413.9927.

Ethyl 2-bromo-9-(2,5-dimethylthiophen-3-yl)-7-hydroxy-6-oxo-6*H*-benzo[*c*]chromene-8-carboxylate (40). Reaction of **1k** (337 mg, 1.0 mmol) and β-ketoester **2d** (216 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **40** (207 mg, 64%) as a solid: mp 203–205 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6, 164.4, 159.7, 149.8, 145.3, 136.5, 135.0, 134.4, 134.2, 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^{-1}; HRMS m/z (M^+) calcd for $C_{22}H_{17}BrO_5S$: 471.9980. Found: 471.9982.

7-Hydroxy-9-(naphthalen-2-yl)-6*H*-benzo[*c*]chromen-6-one (41). Reaction of **1l** (274 mg, 1.0 mmol) and β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **41** (212 mg, 63%) as a solid: mp 228–230 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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,

117.9, 113.5, 104.8; IR (KBr) 3422, 2370, 1683, 1620, 1557, 1272, 1081, 858, 755 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{23}H_{14}O_3$: 338.0943. Found: 338.0943.

7-Hydroxy-8-methyl-9-(naphthalen-2-yl)-6*H*-benzo[*c*]chromen-6-one (42). Reaction of **1l** (274 mg, 1.0 mmol) and β-ketoester **2b** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **42** (179 mg, 51%) as a solid: mp 194–196 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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), 2.17 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{24}H_{16}O_3$: 352.1099. Found: 352.1097.

7-Hydroxy-9-(naphthalen-2-yl)-8-phenyl-6*H*-benzo[*c*]chromen-6-one (43). Reaction of **1l** (274 mg, 1.0 mmol) and β-ketoester **2c** (288 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **43** (207 mg, 50%) as a solid: mp 199–201 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{29}H_{18}O_3$: 414.1256. Found: 414.1254.

9-Cyclopropyl-7-hydroxy-6*H*-benzo[*c*]chromen-6-one (44). Reaction of **1m** (188 mg, 1.0 mmol) and β-ketoester **2a** (195 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **44** (181 mg, 72%) as a solid: mp 140–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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 (1H, m), 1.12–1.04 (2H, m), 0.85–0.78 (2H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{16}H_{12}O_3$: 252.0786. Found: 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 β-ketoester **2c** (288 mg, 1.5 mmol) using Cs_2CO_3 (650 mg, 2.0 mmol) afforded **45** (200 mg, 61%) as a solid: mp 187–190 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{22}H_{16}O_3$: 328.1099. Found: 328.1100.

General procedure for the synthesis of terphenyls (49–54)

To a solution of KOH (2.0 mmol) in DMSO (3.5 mL) and water (0.5 mL), CH_3I (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 monitored 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. 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 methyl 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; ^{1}H NMR (300 MHz, $CDCl_3$) 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 (3H, s), 1.66 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{24}H_{24}O_4$: 376.1675. 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; ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75 MHz, $CDCl_3$) 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, 1712, 1614, 1548, 1405, 1273, 1163, 749 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{23}H_{21}BrO_4$: 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; ^{1}H NMR (300 MHz, $CDCl_3$) 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, m), 3.86 (3H, s), 3.79 (3H, s), 3.70 (3H, s), 3.57 (3H, s), 3.38 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{30}H_{28}O_6$: 484.1886. Found: 384.1886.

Methyl 5′-bromo-5-(2,5-dimethylthiophen-3-yl)-2′,3-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 solid: mp 140–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 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); ^{13}C NMR (75 MHz, $CDCl_3$) δ 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^{-1}; HRMS *m/z* (M^+) calcd for $C_{22}H_{21}BrO_4S$: 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; ^{1}H NMR (300 MHz, $CDCl_3$) 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, $CDCl_3$) δ 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, 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^{-1}; HRMS m/z (M^+) calcd for $C_{27}H_{24}O_4$: 412.1675. Found: 412.1676.

Methyl 5′-cyclopropyl-2,3′-dimethoxy-[1,1′:4′,1″-terphenyl]-2′-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; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.18 (7H, m), 6.94 (1H, d, J = 7.5 Hz), 6.87 (1H, d, J = 8.4 Hz), 6.61 (1H, s), 3.71 (3H, s), 3.54 (3H, s), 3.32 (1H, s), 1.68–1.59 (1H, m), 0.74–0.61 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) 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, 2942, 2842, 1731, 1604, 1544, 1280, 1143, 1022, 757, 706 cm^{-1}; HRMS m/z (M^+) calcd for $C_{25}H_{24}O_4$: 388.1675. Found: 388.1673.

Crystal refinement data for compound 26

$C_{44}H_{36}O_6$, 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^3, Z = 2, T = 200(2) K, ρ_{calcd} = 1.335 mg m^{-3}, $2\theta_{max.}$ = 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 [$I > 2\sigma(I)$], wR_2 = 0.2354 (all data) and S = 1.030 with the largest difference peak and hole of 0.307 and −0.429 e Å^{-3} respectively.

Acknowledgements

This work was supported by the 2013 Yeungnam University Research Grant (213A367018).

Notes and references

1 (*a*) L. F. Tietze and U. Beifuss, *Angew. Chem., Int. Ed.*, 1993, **105**, 137; (*b*) L. F. Tietze, G. Brasche and K. M. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, 2006.

2 (*a*) K. C. Nicolaou, D. J. Edmonds and P. G. Bulger, *Angew. Chem., Int. Ed.*, 2006, **45**, 7134; (*b*) K. C. Nicolaou, P. G. Bulger and D. Sarlah, *Angew. Chem., Int. Ed.*, 2005, **44**, 4442; (*c*) I. Hayato, S. Takaki and H. Yujiro, *Angew. Chem., Int. Ed.*, 2009, **48**, 1304.

3 (*a*) Y. L. Garazd, A. S. Ogorodniichuk, M. M. Garazd and V. P. Khilya, *Chem. Nat. Compd.*, 2003, **38**, 424; (*b*) K. Ishiguro, M. Yamaki, M. Kashihara, S. Takagi and K. Isoi, *Phytochemistry*, 1990, **29**, 1010; (*c*) H. Abe, K. Nishioka, S. Takeda, M. Arai, Y. Takeuchi and T. Harayama, *Tetrahedron Lett.*, 2005, **46**, 3197; (*d*) K. Koch, J. Podlech, E. Pfeiffer and M. Metzler, *J. Org. Chem.*, 2005, **70**, 3275; (*e*) H. Raistrick, C. E. Stickings and R. Thomas, *Biochemistry*, 1953, **55**, 421; (*f*) R. W. Pero, D. Harvan and M. C. Blois, *Tetrahedron Lett.*, 1973, 945.

4 (*a*) T. Hosoya, E. Takashiro, T. Matsumoto and K. Suzuki, *J. Am. Chem. Soc.*, 1994, **116**, 1004; (*b*) C. A. James and V. Snieckus, *Tetrahedron Lett.*, 1997, **38**, 8149.

5 (*a*) J. M. Schmidt, G. B. Tremblay, M. Page, J. Mercure, M. Feher, R. Dunn-Dufault, M. G. Peter and P. R. Redden, *J. Med. Chem.*, 2003, **46**, 1289; (*b*) J. Pandey, A. K. Jha and K. Hajela, *Bioorg. Med. Chem.*, 2004, **12**, 2239.

6 (*a*) J. P. Edwards, S. J. West, K. B. Marschke, D. E. Mais, M. Gottardis and T. K. Jones, *J. Med. Chem.*, 1998, **41**, 303; (*b*) M. J. Coghlan, P. R. Kym, S. W. Elmore, A. X. Wang, J. R. Luly, D. Wilcox, M. Stashko, C. W. Lin, J. Miner, C. Tyree, M. Nakane, P. Jacobson and N. C. Lane, *J. Med. Chem.*, 2001, **44**, 2879.

7 B. Appel, N. N. R. Salesh and P. Langer, *Chem.–Eur. J.*, 2006, **12**, 1221.

8 R. Myrray, J. Mendez and S. Brown, *The Natural Coumarins: Occurrence, Chemistry and Biochemistry*, John Wiley & Sons, New York, 1982, pp. 97–111.

9 (*a*) W. T. L. Sidwell, H. Fritz and C. Tamm, *Helv. Chim. Acta*, 1971, **54**, 207; (*b*) K. Koch, J. Podlech, E. Pfeiffer and M. Metzler, *J. Org. Chem.*, 2005, **70**, 3275; (*c*) R. J. Cole and R. H. Cox, *Handbook of Toxic Fungal Metabolites*, Academic Press, New York, 1981, p. 614; (*d*) N. Tan, Y. Tao, J. Pan, S. Wang, F. Xu, Z. She, Y. Lin and E. B. G. Jones, *Chem. Nat. Compd.*, 2008, **44**, 296; (*e*) W. Gu, *World J. Microbiol. Biotechnol.*, 2009, **25**, 1677; (*f*) T. Matsumoto, T. Hosoya and H. Shigemori, *Heterocycles*, 2010, **81**, 1231; (*g*) X. Meng, Z. Mao, J. Lou, L. Xu, L. Zhong, Y. Peng, L. Zhou and M. Wang, *Molecules*, 2012, **17**, 11303.

10 (*a*) T. Tanahashi, M. Kuroishi, A. Kuwahara, N. Nagakura and N. Hamada, *Chem. Pharm. Bull.*, 1997, **45**, 1183; (*b*) N. Hamada, T. Tanahashi, S. Goldsmith and T. H. Nash III, *Symbiosis*, 1997, **23**, 219; (*c*) N. Hamada, T. Tanahashi, H. Miyagawa and H. Miyawaki, *Symbiosis*, 2001, **31**, 23; (*d*) T. Tanahashi, Y. Takenaka, N. Nagakura and N. Hamada, *Phytochemistry*, 2003, **62**, 71; (*e*) E. Hormazabal, G. Schmeda-Hirschmann, L. Astudillo, J. Rodriguez, C. Z. Theoduloz and C. Naturforsch, *BioScience*, 2005, **60**, 11; (*f*) I. Kock, K. Krohn, H. Egold, S. Dreager, B. Schulz and J. Rheinheimer, *Eur. J. Org. Chem.*, 2007, 2186.

11 (*a*) U. Holler, A. D. Wright, G. F. Matthee, G. M. Konig, S. Draeger, H. J. Aust and B. Schulz, *Mycol. Res.*, 2000, **104**, 1354; (*b*) Y. C. Song, W. Y. Huang, C. Sun, F. W. Wang and R. X. Tan, *Biol. Pharm. Bull.*, 2005, **28**, 506.

12 N. Kim, M.-J. Sohn, C.-J. Kim, H. J. Kwon and W.-G. Kim, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 2503.
13 (*a*) P. Pahari, M. K. Kharel, M. D. Shepherd, S. G. van Lanen and J. Rohr, *Angew. Chem., Int. Ed.*, 2012, **51**, 1216; (*b*) N. Tibrewal, P. Pahari, G. Wang, M. K. Kharel, C. Morris, T. Downey, Y. Hou, T. S. Bugni and J. Rohr, *J. Am. Chem. Soc.*, 2012, **134**, 18181; (*c*) L. R. McGee and P. N. Confalone, *J. Org. Chem.*, 1988, **53**, 3695; (*d*) D. J. Hart and A. Mannino, *Tetrahedron*, 1996, **52**, 3841; (*e*) C. Fischer, F. Lipata and J. Rohr, *J. Am. Chem. Soc.*, 2003, **125**, 7818; (*f*) K. Suzuki, *Pure Appl. Chem.*, 2000, **72**, 1783; (*g*) I. Takemura, K. Imura, T. Matsumoto and K. Suzuki, *Org. Lett.*, 2004, **6**, 2503; (*h*) N. Yamashita, K. Shin-Ya, K. Furihata, Y. Hayakawa and H. Seto, *J. Antibiot.*, 1998, **51**, 1105.
14 (*a*) Q. J. Zhou, K. Worm and R. E. Dolle, *J. Org. Chem.*, 2004, **69**, 5147; (*b*) G. J. Kemperman, B. Ter Horst, D. Van de Goor, T. Roeters, J. Bergwerff, R. Van der Eem and J. Basten, *Eur. J. Org. Chem.*, 2006, 3169; (*c*) I. Hussain, V. T. H. Nguyen, M. A. Yawer, T. T. Dang, C. Fiscer, H. Reinke and P. Langer, *J. Org. Chem.*, 2007, **72**, 6255; (*d*) E. J. Carlson, A. M. S. Riel and B. J. Dahl, *Tetrahedron Lett.*, 2012, **53**, 6245; (*e*) N. Thasana, R. Worayuthakarn, P. Kradanrat, E. Hohn, L. Young and S. Ruchirawat, *J. Org. Chem.*, 2007, **72**, 9379.
15 M. E. Jung and D. A. Allen, *Org. Lett.*, 2009, **11**, 757.
16 R. Singha, S. Roy, S. Nandi, P. Ray and J. K. Ray, *Tetrahedron Lett.*, 2013, **54**, 657.
17 J. Luo, Y. Lu, S. Liu, J. Liu and G. J. Deng, *Adv. Synth. Catal.*, 2011, **353**, 2604.
18 (*a*) U. Sankar, C. Raju and R. Uma, *Curr. Chem. Lett.*, 2012, **1**, 123; (*b*) R. N. Salvatore, A. S. Nagle and K. W. Jung, *J. Org. Chem.*, 2002, **67**, 674; (*c*) G. D. Cuny, *Tetrahedron Lett.*, 2003, **44**, 8149.
19 J. K. Liu, *Chem. Rev.*, 2006, **106**, 2209.
20 (*a*) D. Simoni, R. Rondanin, R. Baruchello, M. Rizzi, G. Grisolia, M. Eleopra, S. Grimaudo, A. Di Cristina, M. R. Pipitone, M. R. Bongiorno, M. Arico, F. P. Invidiata and M. Tolomeo, *J. Med. Chem.*, 2008, **51**, 4796; (*b*) H. Kikuchi, Y. Matsuo, Y. Katou, Y. Kubohara and Y. Oshima, *Tetrahedron*, 2012, **68**, 8884.
21 (*a*) K. Mullen and G. Wegner, *Electronic Materials: The Oligomer Approach*, Wiley-VCH, Weinhein, Germany, 1988; (*b*) B. Chen, U. Baumeister, G. Pelzl, M. K. Das, X. Zeng, G. Ungar and C. Tschierske, *J. Am. Chem. Soc.*, 2005, **127**, 16578; (*c*) R. S. Wright and T. K. Vinod, *Tetrahedron Lett.*, 2003, **44**, 7129; (*d*) B. S. Udayakumar and G. B. Schuster, *J. Org. Chem.*, 1992, **57**, 348.
22 (*a*) K. Kawada, A. Arimura, T. Tsuri, M. Fuji, T. Komurasaki, S. Yonezawa, A. Kugimiya, N. Haga, S. Mitsumori, M. Inagaki, T. Nakatani, Y. Tamura, S. Takechi, T. Taishi, J. Kishino and M. Ohtani, *Angew. Chem., Int. Ed.*, 1998, **37**, 973; (*b*) M. Albrecht and M. Schneider, *Synthesis*, 2000, 1557; (*c*) C. J. J. Wu, C. Xue, Y.-M. Kuo and F.-T. Luo, *Tetrahedron*, 2005, **61**, 4735; (*d*) N. Hayashi, T. Yoshikawa, T. Ohnuma, H. Higuchi, K. Sako and H. Uekusa, *Org. Lett.*, 2007, **9**, 5417; (*e*) D. W. Lin, T. Masuda, M. B. Biskup, J. D. Nelson and P. S. Baran, *J. Org. Chem.*, 2011, **76**, 1013; (*f*) L. A. Adrio, J. M. A. Miguez and K. K. Hii, *Org. Prep. Proced. Int.*, 2009, **41**, 331.
23 G. Monzon and P. Knochel, *Synlett*, 2010, 304.
24 (*a*) A. de Meijere and F. Diederich, *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH, Weinheim, 2nd edn, 2004; (*b*) N. Miyaura, *Cross-Coupling Reactions. Topics in Current Chemistry*, Springr, Berlin, vol. 219, 2002.
25 (*a*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457; (*b*) A. Suzuki, *J. Organomet. Chem.*, 2002, **653**, 83; (*c*) V. Polshettiwar, A. Decottignies, C. Len and A. Fihri, *ChemSusChem*, 2010, **3**, 502; (*d*) A. Molnar, *Chem. Rev.*, 2011, **111**, 2251; (*e*) C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacotand and V. Snieckus, *Angew. Chem., Int. Ed.*, 2012, **51**, 5062.
26 P. Garcia-Garcia, M. A. Fernandez-Rodriguez and E. Aguilar, *Angew. Chem., Int. Ed.*, 2009, **48**, 5534.
27 W. Liu, H. Cao, H. Zhang, H. Zhang, K. H. Chung, C. He, H. Wang, F. Y. Kwong and A. Lei, *J. Am. Chem. Soc.*, 2010, **132**, 16737.
28 Y. Shibata and K. Tanaka, *Synthesis*, 2012, 323.

