Tetrahedron 71 (2015) 5137–5147

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Pd-catalyzed cross-coupling study of bi-functional 3-bromo-4-trifloxycoumarins with triarylbismuth reagents

Maddali L.N. Rao *, Abhijeet Kumar

Department of Chemistry, Indian Institute of Technology Kanpur, Kanpur 208 016, India

ARTICLE INFO

Article history:
Received 8 January 2015
Received in revised form 14 May 2015
Accepted 18 May 2015
Available online 22 May 2015

Keywords:
Pd-catalyzed
Cross-coupling
Triarylbismuth
3-Bromo-4-trifloxycoumarin
3-Bromo-4-arylcoumarin
3,4-Diarylcoumarin

ABSTRACT

The cross-coupling reactions of functionalized 3-bromo-4-trifloxycoumarins have been explored with threefold arylating triarylbismuth reagents. These palladium-catalyzed reactions afforded chemo-selective C-4 arylations with the facile formation of 3-bromo-4-arylcoumarins in good to high yields. Additionally, palladium-catalyzed arylations of functionalized 3-bromo-4-arylcoumarins also participated in the second arylation to give functionalized 3,4-diarylcoumarins in high yields.

1. Introduction

Coumarin scaffolds are prevalent in various plant species[1] and are popular with a vast range of biological and medicinal properties.[2] Arylated coumarins in particular, are precursors for various biologically active drug molecular skeletons.[3] The development of new and viable synthetic methods for functionalized coumarins is vital and of general interest, as this will augment studies using coumarins for various medicinal and other applications.[3,4] Transition metal catalyzed reactions have been extensively used for the arylation of coumarin skeletons.[5,6] Recently, we too have reported the Pd-catalyzed synthesis of 4-arylcoumarins using triarylbismuth reagents as threefold arylating agents.[7,8] In continuation, we have explored the novel reactivity of 3-bromo-4-trifloxycoumarin and its other bromide derivatives (Fig. 1) with triarylbismuth reagents.

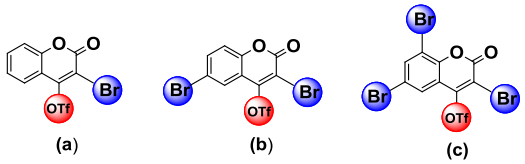
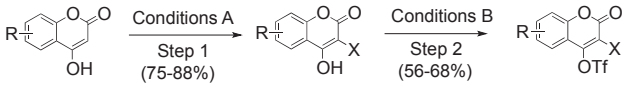


Fig. 1. Coumarin skeletons with reactive functionality.

These efforts gave the opportunity for chemo-selective couplings of 3-bromo-4-trifloxycoumarins and their bis-coupling studies under palladium-catalyzed conditions as outlined here.

2. Results and discussion

To start this coupling study, the required 3-halo-4-trifloxycoumarins have been prepared from 4-hydroxycoumarins as given in Scheme 1.[6a,9]



1a, R = H; **1b**, R = 6-Ph; **1c**, R = 7,8-Benzofused;
1d, R = 6-Br; **1e**, R = 6,8-Dibromo; **1f**, R = H

Conditions A: NBS or NCS (1.05 equiv), NH_4OAc (0.1 equiv), MeCN, rt, 3-10 h
Conditions B: Tf_2O (1.5 equiv), Et_3N (1.2 equiv), CH_2Cl_2, 0 °C - rt, 10 h

Scheme 1. Synthesis of 3-halo-4-trifloxycoumarins.

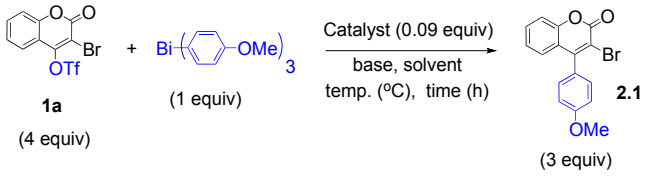
It was of interest to explore the competitive coupling reactivity of bi-functional 3-bromo-4-trifloxycoumarins in the context of facile couplings witnessed vide supra using 4-bromo, 4-chloro and 4-trifloxycoumarin derivatives and triarylbismuth reagents. To understand the bi-functional coupling reactivity of 3-bromo-4-trifloxycoumarin, it was tested with tri(*p*-anisyl)bismuth as

* Corresponding author. Tel./fax: +91 512 2597532; e-mail address: maddali@iitk.ac.in (M.L.N. Rao).

http://dx.doi.org/10.1016/j.tet.2015.05.060
0040-4020/

summarized in Table 1. The reactivity of 3.3 equiv of 3-bromo-4-trifloxycoumarin was initially studied with 1 equiv of tri(*p*-anisyl) bismuth using $PdCl_2(PPh_3)_2$ (0.09 equiv), K_3PO_4 (1 equiv) in DMA at 90 °C for 2 h and this testing provided selective coupling at triflate terminus to give chemo-selectively coupled 3-bromo-4-(4-methoxyphenyl)-2*H*-chromen-2-one (**2.1**) in 50% yield (Entry 1, Table 1). It was further tested with bases involving KOAc, Na_2CO_3 and $NaHCO_3$ to check their utility to improve the yield (Entries 2–4, Table 1). From this, the reaction with $NaHCO_3$ showed a marginal improvement up to 58% yield. Importantly, we have observed the hydrolysis of triflate terminus and the corresponding 4-hydroxycoumarin was observed in minor amount at the end of the reaction. To circumvent this problem, the coupling was tested with 4 equiv of **1a** and this showed the improvement to afford 66% yield (Entry 5, Table 1).

Table 1
Screening conditions[a,b]



Entry	Catalyst	Base (equiv)	Solvent	Yield (%)
1	$PdCl_2(PPh_3)_2$	K_3PO_4 (1)	DMA	50[c]
2	$PdCl_2(PPh_3)_2$	KOAc (1)	DMA	45[c]
3	$PdCl_2(PPh_3)_2$	Na_2CO_3 (1)	DMA	56[c]
4	$PdCl_2(PPh_3)_2$	$NaHCO_3$ (1)	DMA	58[c]
5	$PdCl_2(PPh_3)_2$	$NaHCO_3$ (1)	DMA	66
6	$Pd(PPh_3)_4$	$NaHCO_3$ (1)	DMA	67
7	$Pd(OAc)_2/4PPh_3$	$NaHCO_3$ (1)	DMA	52
8	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	DMA	77
9	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	DMF	58
10	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	NMP	69
11	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (2)	DMA	52
12	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (0.5)	DMA	60
13	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	DMA	62[d]
14	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	DMA	65[e]
15	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	DMA	58[f]
16	$Pd(OAc)_2(Cy_2NH)_2$	$NaHCO_3$ (1)	DMA	67[g]
17	$Pd(OAc)_2(Cy_2NH)_2$	—	DMA	56
18	—	$NaHCO_3$ (1)	DMA	—

[a] Reaction conditions: **1a** (0.5 mmol, 4 equiv), tri(*p*-anisyl)bismuth (0.125 mmol, 1 equiv), $Pd(OAc)_2(Cy_2NH)_2$ (0.011 mmol, 0.09 equiv), base (0.125 mmol, 1 equiv), DMA (3 mL), 2 h, 90 °C.
[b] Isolated yields based on three aryl coupling from $BiAr_3$; bianisyl formed in 5–22% amounts.
[c] With **1a** in 3.3 equiv (0.412 mmol).
[d] At 60 °C.
[e] At 100 °C.
[f] With1 h.
[g] With 0.05 equiv catalyst.

Additional check with different catalyst precursors (Entries 6–8, Table 1) revealed the better performance with $Pd(OAc)_2(Cy_2NH)_2$ and in this case 77% yield was obtained (Entry 8, Table 1). Further study in DMF or NMP did not improve the yield (Entries 9 and 10, Table 1). Further scrutiny with base, temperature, catalyst and time (Entries 11–18, Table 1) gave additional clarity of the overall requirement for better coupling reactivity. This made us to consider the combination with $Pd(OAc)_2(Cy_2NH)_2$ (0.09 equiv) and $NaHCO_3$ (1 equiv) in DMA at 90 °C for 2 h as the most effective (Entry 8, Table 1) to achieve high cross-coupling yield with chemo-selective coupling.

The generality of these couplings was further investigated with divergent 3-bromo-4-trifloxycoumarins and triarylbismuths under established coupling conditions (Table 2). This evaluation demonstrated excellent consistency in terms of chemo-selective coupling from organic electrophile and threefold coupling of triarylbismuths to deliver high yields. In general, the couplings of **1a** with electronically different triarylbismuths proved to be more efficient with arylations selectively at 4-position. This reactivity gave the respective 3-bromo-4-arylcoumarins (**2.1**–**2.10**) in 63–88% yields (Entries 1–10, Table 2). In particular, the coupling reaction carried out with 4-CF_3 substituted $BiPh_3$ reacted somewhat poorly and gave 2.11 in 36% yield (Entry 11, Table 2). The broadness of the established protocol was further tested with electronically different 3-bromo-6-phenyl-4-trifloxycoumarin (**1b**), 7,8-benzofused 3-bromo-4-trifloxycoumarin (**1c**), 3,6-dibromo-4-trifloxycoumarin (**1d**) and 3,6,8-tribromo-4-trifloxycoumarin (**1e**) substrates. It was planned to explore the respective chemo-selective coupling reactivity of these substrates with triarylbismuth reagents. Under the established conditions, the reactions of **1b** and **1c** gave coupling products (**2.12**–**2.22**) in 60–86% yields (Entries 12–22, Table 2). The reactivity tested with **1d** and **1e** with additional bromo substitutions provided the selective couplings at C-4 position with the formation of 3,6-dibromo-4-arylcoumarins (**2.23**–**2.26**) and 3,6,8-tribromo-4-arylcoumarins (**2.27**–**2.29**) in 61–74% yields (Entries 23–29, Table 2). One of these products, 3,6-dibromo-4-*p*-tolyl-2*H*-chromen-2-one (**2.23**) was crystallized out and found to be suitable for single X-ray crystal analysis (Fig. 2). This further established unambiguously the selective arylation at 4-position. Finally, the formation of diverse 3-bromo-4-arylcoumarins in good to excellent yields was witnessed from chemo-selective arylation of 3-bromo-4-trifloxycoumarins with the optimized conditions. The chemo-selective couplings leaving 3-bromo group intact allows further functionalizations.[4,10]

Having successfully established chemo-selective couplings at 4-position, it was of interest to further functionalize 3-bromo-4-arylcoumarin with triarylbismuth reagents. To check this feasibility, a brief screening was carried out using earlier established conditions (Scheme 2).

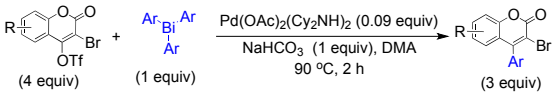
Under the conditions tested, the desired arylation at 3-bromo position took place moderately with the formation of 3,4-bis(4-methoxyphenyl)-2*H*-chromen-2-one (**3.1**) in 53% yield. The applied conditions with 4 h duration furnished 60% yield, while the heating at 110 °C for 2 h afforded 73% yield. The bis-coupling yield was further improved to 80% at 110 °C, 4 h condition. It was satisfying to realize that the optimized protocol established for chemo-selective couplings was found to be appropriate for second arylation with slight modification in reaction temperature and time to furnish high yield.

The 3-bromo arylation was carried out with different 3-bromo-4-arylcoumarins and $BiAr_3$ reagents. The effective second arylations were witnessed with the formation of 3,4-diarylcoumarins (**3.1**–**3.12**) (Entries 1–12, Table 3) in 61–80% yields. These couplings carried with different $BiAr_3$ reagents furnished both symmetrically and unsymmetrically substituted 3,4-diarylcoumarins in good to high yields.

In addition, the bis-arylated 3,4-bis (4-methoxyphenyl)-2*H*-chromen-2-one (**3.1**) was measured by single X-ray crystal analysis (Fig. 3). The optimized conditions thus allowed the synthesis of various 3,4-diarylcoumarins in a facile manner. The practical utility of these products is high as some of the hybrid derivatives of 3,4-diarylcoumarins have been reported to exhibit DNA-binding and anti-proliferative activities.[11] Further, some diarylated coumarin analogues were studied as estrogen receptor modulators.[12] The corresponding 3,4-diarylchromanes have been explored as estrogen agonists.[13]

In continuation, the synthesis of symmetrically substituted 3,4-diarylcoumarin (**3.1**) was attempted in one pot operation (Scheme 3). However, under the conditions employed, the exclusive arylation at C-4 position was obtained with the formation of **2.1** in 79% yield. The corresponding bis-arylated product **3.1** was not formed

Table 2
Pd-catalyzed chemo-selective couplings with 3-bromo-4-trifloxycoumarins and $BiAr_3$ reagents[a,b]



Entry	3-Bromo-4-trifloxy coumarin	Ar_3Bi	3-Bromo-4-aryl coumarin	Yield (%)	Entry	3-Bromo-4-trifloxy coumarin	Ar_3Bi	3-Bromo-4-aryl coumarin	Yield (%)
1	**1a**	$Bi(C_6H_4OMe)_3$	**2.1**	77	16	**1b**	$Bi(C_6H_4O^iPr)_3$	**2.16**	79
2	**1a**	$BiPh_3$	**2.2**	84	17	**1b**	$Bi(C_6H_4F)_3$	**2.17**	60
3	**1a**	$Bi(C_6H_4Me)_3$	**2.3**	88	18	**1c**	$Bi(C_6H_4Me)_3$	**2.18**	72
4	**1a**	$Bi(C_6H_4OMe)_3$	**2.4**	64	19	**1c**	$BiPh_3$	**2.19**	62
5	**1a**	$Bi(C_6H_3(OMe)_2)_3$	**2.5**	76	20	**1c**	$Bi(C_6H_4OMe)_3$	**2.20**	70
6	**1a**	$Bi(C_6H_4OEt)_3$	**2.6**	73	21	**1c**	$Bi(C_6H_4OEt)_3$	**2.21**	82
7	**1a**	$Bi(C_6H_4F)_3$	**2.7**	64	22	**1c**	$Bi(C_6H_4O^iPr)_3$	**2.22**	86
8	**1a**	$Bi(C_6H_4O^iPr)_3$	**2.8**	82	23	**1d**	$Bi(C_6H_4Me)_3$	**2.23**	72
9	**1a**	$Bi(C_6H_4Cl)_3$	**2.9**	63	24	**1d**	$Bi(C_6H_4OMe)_3$	**2.24**	71
10	**1a**	$Bi(C_6H_4O^nBu)_3$	**2.10**	74	25	**1d**	$Bi(C_6H_4OEt)_3$	**2.25**	74
11	**1a**	$Bi(C_6H_4CF_3)_3$	**2.11**	36	26	**1d**	$Bi(C_6H_4O^iPr)_3$	**2.26**	72
12	**1b**	$Bi(C_6H_4OMe)_3$	**2.12**	78	27	**1e**	$Bi(C_6H_4OMe)_3$	**2.27**	61
13	**1b**	$Bi(C_6H_4Me)_3$	**2.13**	74	28	**1e**	$Bi(C_6H_4O^iPr)_3$	**2.28**	67
14	**1b**	$Bi(C_6H_4OEt)_3$	**2.14**	81	29	**1e**	$Bi(C_6H_4Me)_3$	**2.29**	68
15	**1b**	$Bi(C_6H_4Me)_3$	**2.15**	70					

[a] Reaction conditions: **1a-1e** (0.5 mmol, 4 equiv), Ar_3Bi (0.125 mmol, 1 equiv), $Pd(OAc)_2(Cy_2NH)_2$ (0.011 mmol, 0.09 equiv), $NaHCO_3$ (0.125 mmol, 1 equiv), and DMA (3 mL), 90 °C, 2 h. [b] Isolated yields based on threefold coupling from Ar_3Bi reagents; biaryls formed in 5-16% amounts.

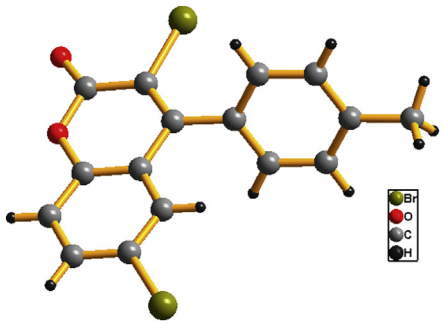
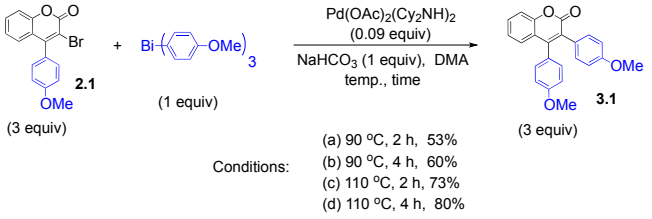


Fig. 2. Crystal structure of **2.23** (CCDC No.1059353).



Scheme 2. Screening for arylation at 3-bromo position.

in this reaction. From this, it was clear that further modification of the coupling conditions is necessary to achieve the one-pot bis-arylation using 3-bromo-4-trifloxycoumarin.

We also attempted the synthesis of triarylated coumarin by exploiting the differential reactivity with different bromide substitutions. For example, the sequential arylation of 3,6-dibromo-4-(4-methoxyphenyl)-2*H*-chromen-2-one (**2.24**) was attempted (Scheme 4).

Initially, the arylation at arylbromide terminus was carried out with tri(*p*-isopropoxyphenyl)bismuth using $PdCl_2(PPh_3)_2$ with KOAc in DMF at 90 °C to afford **4.1** in 60% yield (Conditions A, Scheme 4).[7] In the next step, it was further cross-coupled with tri(*p*-ethoxyphenyl)bismuth under the conditions established (Conditions B, Scheme 4). This endeavor furnished 3,4,6-triarylated coumarin **4.2** in 65% yield. The synthesis of triarylated coumarin under different conditions demonstrates the selective and practicable nature of our cross-coupling methodology under different reaction conditions.

At this stage we were curious to test the coupling reactivity of 3-chloro-4-trifloxycoumarin as given in Scheme 5. Under our established conditions, this reaction afforded **5.1** in 39% yield as chemo-selective coupling product. Further attempt to convert 5.1 to the corresponding 3,4-diarylcoumarin (**3.1**) under the conditions employed for second arylation (Table 3) did not afford the product.

It is to be highlighted that the coupling reactions carried out in the present study with tiarylbismuth reagents has threefold coupling advantage in comparison to similar couplings reported with arylboronic acids[6a] for the functionalization of 3-bromo-4-trifloxycoumarin under palladium coupling conditions. In couplings with arylboronic acids two different catalytic protocols were needed to achieve bis-arylations of 3-bromo-4-trifloxycoumarin to obtain 3,4-diarylcoumarin via 3-bromo-4-arylcoumarin. However, in our case it was essentially one protocol conditions but with simpler modification of reaction temperature adopted with established protocol conditions for the second arylation step. Overall, the reactivity unleashed with triarylbismuth reagents showed broad applicability under the established coupling conditions.

3. Conclusion

We have disclosed an efficient protocol for the chemo-selective synthesis of a library of 3-bromo-4-arylcoumarins using triarylbismuths as threefold arylating partners under palladium coupling conditions. In these couplings, 3-bromo-4-trifloxycoumarins have selectively afforded C-4 arylations in good to high yields. Further, a facile approach for the synthesis of 3,4-diarylcoumarins was demonstrated involving 3-bromo-4-arylcoumarins and bismuth reagents. The work described signifies the facile and robust nature of our methodology with triarylbismuths in structural elaborations leading to mono-, di- and triarylated coumarins. These methods embedded with high practical and synthetic scope are expected to find further applications in organic synthesis.

4. Experimental section

4.1. General remarks

The cross-coupling reactions under palladium conditions have been performed under nitrogen atmosphere in oven dried Schlenk tubes. Literature procedures have been adopted for the synthesis of 3-bromo-4-trifloxycoumarins (**1a**–**1e**)[6a,9] and triarylbismuth compounds.[14] NMR spectra were recorded on JEOL-500 MHz (ECX 500) and JEOL-400 MHz (JNM-ECS) spectrometers. WATERS-Q-Tof Premier-HAB213 and WATERS GCT Premier-CAB155 instruments were used to measure HRMS spectra. Bruker Vector 22 FTIR spectrometer were used to measure IR spectra. Purification of the crude products was carried out using silica gel column chromatography with hexane and ethyl acetate as eluent. Standard drying methods have been applied for purification of solvents.

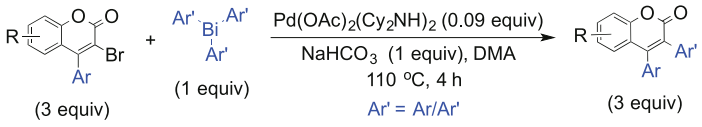
4.2. Representative procedures for compounds 1a–1f

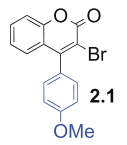
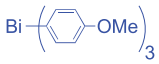
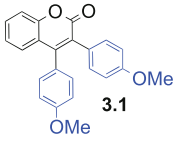
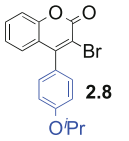
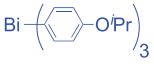
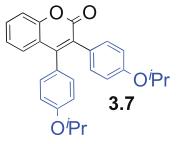
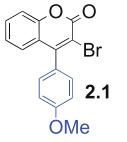
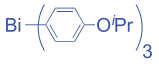
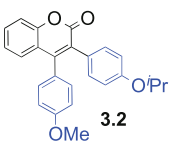
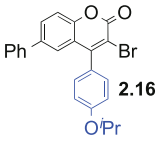
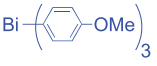
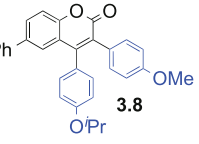
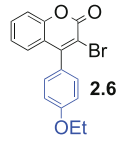
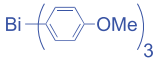
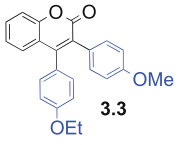
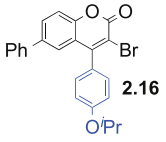
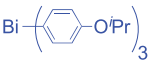
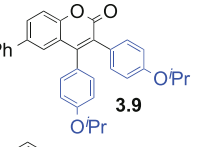
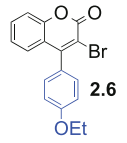
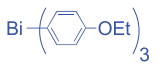
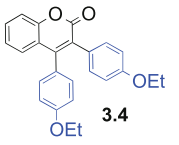
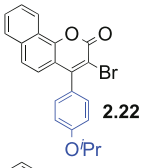
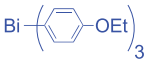
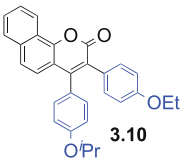
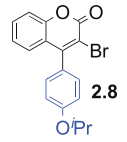
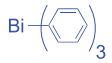
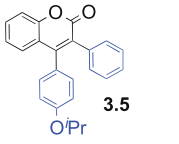
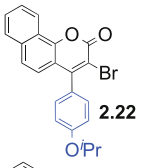
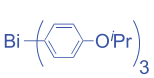
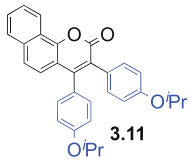
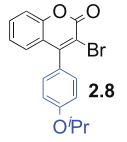
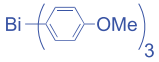
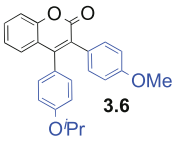
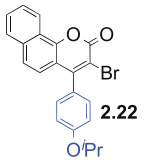
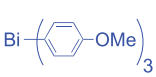
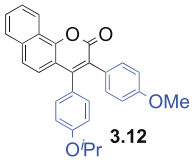
4.2.1. Preparation of 3-bromo-4-hydroxy-2H-chromen-2-one (step1).[9] Bromination of 4-hydroxycoumarin (5 g, 30.8 mmol) was carried out in acetonitrile (100 mL) with the addition of *N*-bromosuccinimide (5.7 g, 32.34 mmol) followed by ammonium acetate (0.237 g, 3.08 mmol). The reaction mixture was stirred at rt for 3 h. After the reaction time, organic solvent was evaporated and the crude was treated with ethyl acetate and water mixture (50 mL, 1:1). The organic layer was extracted with ethyl acetate (3×20 mL), treated with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by crystallization to obtain 3-bromo-4-hydroxycoumarin as light yellow solid (6.5 g, 88%). It was used directly in the next step.

*4.2.2. Preparation of 3-bromo-2-oxo-2H-chromen-4-yl trifluoromethanesulfonate, **1a** (step 2).*[6a] A dried two-neck round bottom flask was charged with 3-bromo-4-hydroxycoumarin (5 g, 20.7 mmol) and dry dichloromethane (100 mL). The mixture was cooled to ice bath temperature. Then triethylamine (3.4 mL, 24.8 mmol) was added and stirred for 5 min followed by triflic anhydride (5.2 mL, 31 mmol) slowly. The resultant mixture was allowed to stir at rt for 10 h. After reaction time, it was quenched with water and extracted with dichloromethane (3×20 mL) and dried over anhydrous $MgSO_4$ and concentrated. It was purified by silica gel column chromatography (2% EtOAc/petroleum ether) to obtain **1a** as white solid (4.8 g, 62%).

*4.2.3. 3-Bromo-2-oxo-2H-chromen-4-yl trifluoromethanesulfo-nate (**1a**).*[6a] White solid (62%); mp 100–102 °C, R_f (10% ethyl acetate in hexane) 0.74; IR (KBr, cm^{-1}): 1746, 1609, 1564, 1429, 1327, 1246, 1210, 1139, 1051, 993, 895, 791, 758, 745, 653, 632, 587; δ_H NMR (500 MHz, $CDCl_3$): 7.76–7.70 (m, 2H, Ar–H), 7.46–7.43 (m, 2H, Ar–H); δ_C NMR (100 MHz, $CDCl_3$): 156.94, 154.79, 151.57, 133.98, 125.61, 122.88, 118.36 (q, J=322.85 Hz), 117.28, 115.20, 107.25; ESI

Table 3
Synthesis of 3,4-diarylated coumarins[a,b]



Entry	3-Bromo-4-aryl coumarin	Ar'_3Bi	3,4-Diarylcoumarin	Yield (%)	Entry	3-Bromo-4-aryl coumarin	Ar'_3Bi	3,4-Diarylcoumarin	Yield (%)
1	 **2.1**		 **3.1**	80	7	 **2.8**		 **3.7**	72
2	 **2.1**		 **3.2**	72	8	 **2.16**		 **3.8**	73
3	 **2.6**		 **3.3**	75	9	 **2.16**		 **3.9**	74
4	 **2.6**		 **3.4**	76	10	 **2.22**		 **3.10**	61
5	 **2.8**		 **3.5**	73	11	 **2.22**		 **3.11**	76
6	 **2.8**		 **3.6**	70	12	 **2.22**		 **3.12**	66

[a] Reaction conditions: 3-Bromo-4-arylcoumarin (0.375 mmol, 3 equiv), Ar'_3Bi (0.125 mmol, 1equiv), $Pd(OAc)_2(Cy_2NH)_2$ (0.011 mmol, 0.09 equiv), $NaHCO_3$ (0.125 mmol, 1 equiv), and DMA (3 mL), 110 °C, 4 h. [b] Isolated yields based on threefold coupling from Ar'_3Bi reagents; biaryls formed 8-15% amounts.

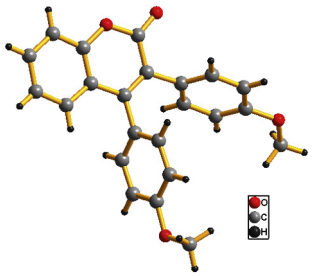
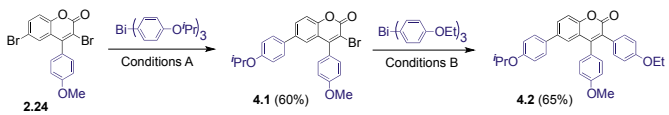
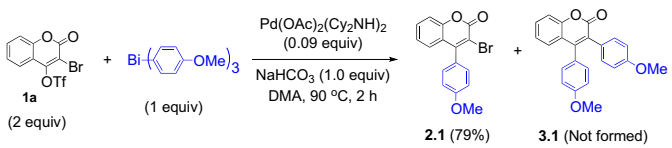


Fig. 3. Crystal structure of **3.1** (CCDC No. 1059354).



Conditions A: Compound **2.24** (0.412 mmol, 3.3 equiv), tri(***p***-isopropoxyphenyl)bismuth (0.125 mmol, 1 equiv), $PdCl_2(PPh_3)_2$ (0.011 mmol, 0.09 equiv), KOAc (0.5 mmol, 4 equiv), DMA (3 mL), 90 °C, 8 h
Conditions B: Compound **4.1** (0.206 mmol, 3.3 equiv), tri(***p***-ethoxyphenyl)bismuth (0.062 mmol, 1 equiv), $Pd(OAc)_2(Cy_2NH)_2$ (0.005 mmol, 0.09 equiv), $NaHCO_3$ (0.062 mmol, 1 equiv), DMA (3 mL), 110 °C, 4 h

Scheme 4. Synthesis of 3,4,6-triarylated coumarin.



Scheme 3. Attempted one-step bis-arylations.

Scheme 5. Cross-coupling with 3-chloro-4-trifloxycoumarin.

(HRMS) (*m*/*z*) calcd for $C_{10}H_8BrF_3NO_5S$ $[M+NH_4]^+$ 389.9259, found: 389.9251.

*4.2.4. 3-Bromo-2-oxo-6-phenyl-2H-chromen-4 trifluoromethanesulfonate (**1b**).* Light yellow solid (65%); mp 118–120 °C, R_f (10% ethyl acetate in hexane) 0.63; IR (KBr, cm^{-1}): 1753, 1618, 1572, 1413, 1228, 1126, 760; δ_H NMR (500 MHz, $CDCl_3$): 7.94–7.91 (m, 2H, Ar–H), 7.58 (d, *J*=7.45 Hz, 2H, Ar–H), 7.53–7.49 (m, 3H, Ar–H), 7.43 (t, *J*=7.45 Hz, 1H); δ_C NMR (125 MHz, $CDCl_3$): 156.97, 154.81, 150.83, 139.09, 138.41, 132.85, 129.28, 128.44, 127.02, 120.92, 118.39 (q, *J*=319.16 Hz), 117.68, 115.44, 107.61; ESI (HRMS) (*m*/*z*) calcd for $C_{16}H_{12}BrF_3NO_5S$ $[M+NH_4]^+$ 465.9572, found: 465.9575.

*4.2.5. 3-Bromo-2-oxo-2H-benzo[h]chromen-4-yl trifluoromethanesulfonate (**1c**).* Light yellow solid (56%); mp 132–134 °C, R_f (10% ethyl acetate in hexane) 0.62; IR (KBr, cm^{-1}): 1741, 1596, 1428, 1232, 1135, 1086, 994, 913, 816, 754, 593; δ_H NMR (500 MHz, $CDCl_3$): 8.53 (d, *J*=8.05 Hz, 1H, Ar–H), 7.92 (d, *J*=8.0 Hz, 1H, Ar–H), 7.81 (d, *J*=9.15 Hz, 1H, Ar–H), 7.76–7.65 (m, 3H, Ar–H); δ_C NMR (100 MHz, $CDCl_3$): 157.24, 155.68, 149.67, 135.40, 130.21, 128.29, 128.08, 125.85, 122.56, 122.33, 118.40 (q, *J*=322.85 Hz), 117.42, 110.71, 106.03; ESI (HRMS) (*m*/*z*) calcd for $C_{14}H_7BrF_3NO_5S$ $[M+H]^+$ 422.9150, found: 422.9141.

*4.2.6. .43,6-Dibromo-2-oxo-2H-chromen-4-yl trifluoromethanesulfonate (**1d**).* White solid (68%); mp 136–138 °C, R_f (10% ethyl acetate in hexane) 0.64; IR (KBr, cm^{-1}): 1739, 1610, 1556, 1419, 1449, 1225, 1130, 1053, 1001, 901, 823, 794, 788, 756, 727, 633, 591; δ_H NMR (500 MHz, $CDCl_3$): 7.84 (d, *J*=2.3 Hz, 1H, Ar–H), 7.80 (dd, *J*=2.02, 8.87 Hz, 1H, Ar–H), 7.34 (d, *J*=8.6 Hz, 1H, Ar–H); δ_C NMR (100 MHz, $CDCl_3$): 156.30, 153.43, 150.34, 136.80, 125.31, 118.97, 118.54, 118.34 (q, *J*=323.17 Hz), 116.66, 108.77; ESI (HRMS) (*m*/*z*) calcd for $C_{10}H_7Br_2F_3NO_5S$ $[M+NH_4]^+$ 469.8343, found: 469.8336.

*4.2.7. 3,6,8-Tribromo-2-oxo-2H-chromen-4-yl trifluoromethanesulfonate (**1e**).* White solid (64%); mp 142–144 °C, R_f (10% ethyl acetate in hexane) 0.80; IR (KBr, cm^{-1}): 1735, 1607, 1548, 1439, 1415, 1298, 1224, 1139, 1071, 1000, 909, 866, 802, 755, 609, 600, 498; δ_H NMR (500 MHz, $CDCl_3$): 8.04 (d, *J*=1.7 Hz, 1H, Ar–H), 7.79 (d, *J*=2.25 Hz, 1H, Ar–H); δ_C NMR (100 MHz, $CDCl_3$): 155.30, 152.91, 147.48, 139.55, 124.52, 118.44, 118.32 (q, *J*=323.17 Hz), 117.50, 112.15, 109.53; ESI (HRMS) (*m*/*z*) calcd for $C_{10}H_6Br_3F_3NO_5S$ $[M+NH_4]^+$ 547.7448, found: 547.7435.

*4.2.8. 3-Chloro-2-oxo-2H-chromen-4-yl trifluoromethane-sulfonate (**1f**).* White solid (64%); mp 88–90 °C, R_f (10% ethyl acetate in hexane) 0.74; IR (KBr, cm^{-1}): 1727, 1604, 1566, 1427, 1347, 1281, 1229, 1133, 1056, 1013, 896, 761, 747, 594; δ_H NMR (400 MHz, $CDCl_3$): 7.74–7.68 (m, 2H, Ar–H), 7.48–7.44 (m, 2H, Ar–H); δ_C NMR (100 MHz, $CDCl_3$): 156.74, 152.26, 150.92, 133.81, 125.71, 122.84, 118.36 (q, *J*=322.53 Hz), 117.29, 116.23, 114.98; EI (HRMS) (*m*/*z*) calcd for $C_{10}H_4ClF_3O_5S$ $[M]^+$ 327.9420, found: 327.9424.

4.3. Representative cross-coupling procedures

*4.3.1. Synthesis of 3-bromo-4-phenyl-2H-chromen-2-one (**2.2**) (Table 2).* A hot-oven dried Schlenk tube was charged with 3-bromo-4-trifloxycoumarin (0.5 mmol, 0.186 g), $BiPh_3$ (0.125 mmol, 0.055 g), $NaHCO_3$ (0.125 mmol, 0.010 g), $Pd(OAc)_2(Cy_2NH)_2$ (0.011 mmol, 0.006 g) and DMA (3 mL) under nitrogen atmosphere. The reaction mixture was stirred in an oil bath at 90 °C for 2 h. At the end of the reaction time, the contents were brought to rt, quenched with water (10 mL) and extracted with ethyl acetate (3×15 mL). The organic extract was treated with brine, dried using $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified on silica gel column chromatography (1% EtOAc/petroleum ether) to obtain compound **2.2** as white solid (0.095 g, 84%). For the yield calculation 0.375 mmol of the product was considered as 100% yield. It was identified by spectroscopic analysis and in comparison with the known data.[6a]

*4.3.2. Synthesis of 3,4-bis(4-methoxyphenyl)-2H-chromen-2-one (**3.1**) (Table 3).* The cross-coupling procedure given in 4.3.1 was adopted using conditions: 3-Bromo-4-(4-methoxyphenyl)-2*H*-chromen-2-one (0.375 mmol, 0.124 g), tri(*p*-anisyl)bismuth (0.125 mmol, 0.066 g), $NaHCO_3$ (0.125 mmol, 0.010 g), $Pd(OAc)_2(Cy_2NH)_2$ (0.011 mmol, 0.006 g), DMA (3 mL), 110 °C, 4 h. The crude product was subjected to silica gel column chromatography (10% EtOAc/petroleum ether) to afford compound **3.1** as white solid (0.108 g, 80%).

*4.3.3. Synthesis of 3-bromo-6-(4-isopropoxyphenyl)-4-(4-methoxyphenyl)-2H-chromen-2one (**4.1**) (Scheme 4).* The cross-coupling procedure given in 4.3.1 was adopted using conditions: Compound **2.24** (0.412 mmol, 0.168 g), tri(*p*-isopropoxyphenyl) bismuth (0.125 mmol, 0.076 g), KOAc (0.5 mmol, 0.049 g), $PdCl_2(PPh_3)_2$ (0.011 mmol, 0.007 g), DMA (3 mL), 90 °C, 8 h. The crude product was purified on silica gel by column chromatography (8% EtOAc/petroleum ether) to afford compound **4.1** as white solid (0.105 g, 60%).

*4.3.4. Synthesis of 3-(4-ethoxyphenyl)-6-(4-isopropoxyphenyl)-4-(4-methoxy-phenyl)-2H-chromen-2-one (**4.2**) (Scheme 4).* The cross-coupling procedure given in 4.3.1 was adopted using conditions: Compound **4.1** (0.206 mmol, 0.095 g), tri(*p*-ethoxyphenyl)bismuth (0.062 mmol, 0.035 g), $NaHCO_3$ (0.062 mmol, 0.005 g), $Pd(OAc)_2(Cy_2NH)_2$ (0.005 mmol, 0.003 g), DMA (3 mL), 110 °C, 4 h. The crude product was purified by silica gel by column chromatography (10% EtOAc/petroleum ether) to afford compound **4.2** as white solid (0.061 g, 65%).

The characterization data for all the cross-coupled products are given below.

*4.3.5. 3-Bromo-4-(4-methoxyphenyl)-2H-chromen-2-one (**2.1**).*[6a] Pale yellow solid (0.096 g, 77%); mp 170–172 °C, R_f (10% ethyl acetate in hexane) 0.31; IR (KBr, cm^{-1}): 1731, 1605, 1507, 1450, 1297, 1273, 1251, 1171, 1034, 983, 810, 755, 626, 587; δ_H NMR (500 MHz, $CDCl_3$): 7.55 (t, *J*=6.72 Hz, 1H, Ar–H), 7.40 (d, *J*=8.55 Hz, 1H, Ar–H), 7.25 (d, *J*=9.15 Hz, 2H, Ar–H), 7.20–7.15 (m, 2H, Ar–H), 7.07 (d, *J*=8.55 Hz, 2H, Ar–H), 3.90 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 160.23, 157.49, 154.49, 152.39, 131.94, 129.72, 127.69, 127.25, 124.62, 120.50, 116.79, 114.16, 112.74, 55.36; ESI (HRMS) (*m*/*z*) calcd for $C_{16}H_{12}BrO_3$ $[M+H]^+$ 330.9970, found: 330.9974.

*4.3.6. 3-Bromo-4-phenyl-2H-chromen-2-one (**2.2**).*[6a] Light yellow solid (0.095 g, 84%); mp 140–142 °C, R_f (10% ethyl acetate in hexane) 0.52; IR (KBr, cm^{-1}): 1728, 1592, 1552, 1446, 1272, 1033, 991, 753, 697, 604; δ_H NMR (500 MHz, $CDCl_3$): 7.58–7.52 (m, 4H, Ar–H), 7.41 (d, *J*=8.3 Hz, 1H, Ar–H), 7.31–7.29 (m, 2H, Ar–H), 7.20–7.17 (m, 1H, Ar–H), 7.08 (dd, *J*=1.42, 8.02 Hz, 1H, Ar–H); δ_C NMR (125 MHz, $CDCl_3$): 157.36, 154.63, 152.47, 135.28, 132.03, 129.35, 128.86, 128.07, 127.61, 124.70, 120.33, 116.83, 112.64; ESI (HRMS) (*m*/*z*) calcd for $C_{15}H_{10}BrO_2$ $[M+H]^+$ 300.9864, found: 300.9867.

*4.3.7. 3-Bromo-4-p-tolyl-2H-chromen-2-one (**2.3**).* Light yellow solid (0.104 g, 88%); mp 158–160 °C, R_f (10% ethyl acetate in hexane) 0.52; IR (KBr, cm^{-1}): 1739, 1723, 1606, 1593, 1508, 1445, 1335, 1273, 1247, 1181, 1038, 987, 806, 751, 732, 624; δ_H NMR (500 MHz, $CDCl_3$): 7.57–7.53 (m, 1H, Ar–H), 7.40–7.36 (m, 3H, Ar–H), 7.20–7.16 (m, 3H, Ar–H), 7.11 (dd, *J*=1.15, 8.05 Hz, 1H, Ar–H), 2.47 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 157.42, 154.79, 152.44, 139.42, 132.29, 131.94, 129.48, 128.03, 127.69, 124.61, 120.44, 116.77, 112.58,

21.43; ESI (HRMS) (*m*/*z*) calcd for $C_{16}H_{12}BrO_2$ $[M+H]^+$ 315.0021, found: 315.0029.

*4.3.8. 3-Bromo-4-(3-methoxyphenyl)-2H-chromen-2-one (**2.4**).* White solid (0.079 g, 64%); mp 138–140 °C, R_f (10% ethyl acetate in hexane) 0.36; IR (KBr, cm^{-1}): 1718, 1588, 1551, 1450, 1346, 1275, 1234, 1030, 998, 790, 754; δ_H NMR (500 MHz, $CDCl_3$): 7.57–7.54 (m, 1H, Ar–H), 7.47 (t, *J*=7.95 Hz, 1H, Ar–H), 7.40 (d, *J*=7.95 Hz, 1H, Ar–H), 7.20–7.17 (m, 1H, Ar–H), 7.11 (d, *J*=7.9 Hz, 1H, Ar–H), 7.06 (d, *J*=7.95 Hz, 1H, Ar–H), 6.87 (d, *J*=7.95 Hz, 1H, Ar–H), 6.82 (s, 1H, Ar–H), 3.85 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 159.80, 157.36, 154.48, 152.42, 136.46, 132.03, 130.10, 127.63, 124.70, 120.20, 116.78, 114.74, 113.67, 112.52, 55.40; ESI (HRMS) (*m*/*z*) calcd for $C_{16}H_{12}BrO_3$ $[M+H]^+$ 330.9970, found: 330.9970.

*4.3.9. 3-Bromo-4-(3,4-dimethoxyphenyl)-2H-chromen-2-one (**2.5**).* Light yellow solid (0.103 g, 76%); mp 142–144 °C, R_f (10% ethyl acetate in hexane) 0.28; IR (KBr, cm^{-1}): 1720, 1605, 1511, 1463, 1349, 1246, 1229, 1137, 1018, 996, 807, 753, 647; δ_H NMR (400 MHz, $CDCl_3$): 7.57–7.53 (m, 1H, Ar–H), 7.39 (d, *J*=8.24 Hz, 1H, Ar–H), 7.22–7.16 (m, 2H, Ar–H), 7.03 (d, *J*=8.24 Hz, 1H, Ar–H), 6.86 (d, *J*=8.68 Hz, 1H, Ar–H), 6.81 (s, 1H, Ar–H), 3.97 (s, 3H), 3.89 (s, 3H); δ_C NMR (100 MHz, $CDCl_3$): 157.43, 154.46, 152.39, 149.67, 149.12, 131.97, 127.68, 127.48, 124.66, 120.91, 120.47, 116.78, 112.74, 111.31, 111.13, 56.07, 55.94; ESI (HRMS) (*m*/*z*) calcd for $C_{17}H_{14}BrO_4$ $[M+H]^+$ 361.0075, found: 361.0079.

*4.3.10. 3-Bromo-4-(4-ethoxyphenyl)-2H-chromen-2-one (**2.6**).* White solid (0.094 g, 73%); mp 140–142 °C, R_f (10% ethyl acetate in hexane) 0.38; IR (KBr, cm^{-1}): 1726, 1609, 1508, 1244, 1176, 1044, 996, 810, 751, 598; δ_H NMR (400 MHz, $CDCl_3$): 7.57–7.53 (m, 1H, Ar–H), 7.40 (d, *J*=8.24 Hz, 1H, Ar–H), 7.26–7.15 (m, 4H, Ar–H), 7.05 (d, *J*=8.68 Hz, 2H, Ar–H), 4.13 (q, *J*=7.17 Hz, 2H), 1.48 (t, *J*=7.1 Hz, 3H); δ_C NMR (100 MHz, $CDCl_3$): 159.71, 157.51, 154.56, 152.45, 131.92, 129.73, 127.73, 127.12, 124.61, 120.57, 116.81, 114.64, 112.76, 63.62, 14.80; ESI (HRMS) (*m*/*z*) calcd for $C_{17}H_{14}BrO_3$ $[M+H]^+$ 345.0126, found: 345.0125.

*4.3.11. 3-Bromo-4-(4-fluorophenyl)-2H-chromen-2-one (**2.7**).* White solid (0.076 g, 64%); mp 126–128 °C, R_f (10% ethyl acetate in hexane) 0.50; IR (KBr, cm^{-1}): 1713, 1605, 1595, 1505, 1344, 1246, 1220, 1160, 1037, 996, 847, 812, 781, 759, 623, 551; δ_H NMR (500 MHz, $CDCl_3$): 7.59–7.55 (m, 1H, Ar–H), 7.41 (d, *J*=8.55 Hz, 1H, Ar–H), 7.31–7.19 (m, 5H, Ar–H), 7.07 (d, *J*=8.55 Hz, 1H, Ar–H); δ_C NMR (125 MHz, $CDCl_3$): 163.07 (d, *J*=248.36 Hz), 157.21, 153.68, 152.39, 132.19, 131.06, 130.22 (d, *J*=8.4 Hz), 127.36, 124.81, 120.20, 116.93, 116.16 (d, *J*=21.6 Hz), 113.08; ESI (HRMS) (*m*/*z*) calcd for $C_{15}H_9BrFO_2$ $[M+H]^+$ 318.9770, found: 318.9776.

*4.3.12. 3-Bromo-4-(4-isopropoxyphenyl)-2H-chromen-2-one (**2.8**).* White solid (0.110 g, 82%); mp 110–112 °C, R_f (10% ethyl acetate in hexane) 0.42; IR (KBr, cm^{-1}): 2977, 1731, 1720, 1608, 1594, 1507, 1450, 1242, 1184, 1122, 1106, 990, 947, 815, 756, 602; δ_H NMR (500 MHz, $CDCl_3$): 7.55–7.53 (m, 1H, Ar–H), 7.40 (d, *J*=8.55 Hz, 1H, Ar–H), 7.23–7.18 (m, 4H, Ar–H), 7.04 (d, *J*=8.55 Hz, 2H, Ar–H), 4.67–4.62 (m, 1H), 1.41 (d, *J*=6.1 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 158.72, 157.52, 154.57, 152.44, 131.89, 129.78, 127.76, 126.87, 124.59, 120.56, 116.79, 115.66, 112.70, 70.05, 22.03; ESI (HRMS) (*m*/*z*) calcd for $C_{18}H_{16}BrO_3$ $[M+H]^+$ 359.0283, found: 359.0284.

*4.3.13. 3-Bromo-4-(4-chlorophenyl)-2H-chromen-2-one (**2.9**).* White solid (0.079 g, 63%); mp 124–126 °C, R_f (10% ethyl acetate in hexane) 0.48; IR (KBr, cm^{-1}): 1733, 1721, 1598, 1485, 1448, 1276, 1246, 1088, 991, 807, 753, 732, 616; δ_H NMR (500 MHz, $CDCl_3$): 7.59–7.54 (m, 3H, Ar–H), 7.41 (d, *J*=7.95 Hz, 1H, Ar–H), 7.26–7.19 (m, 3H, Ar–H), 7.06 (d, *J*=7.95 Hz, 1H, Ar–H); δ_C NMR (125 MHz, $CDCl_3$): 157.10, 153.44, 152.44, 135.60, 133.53, 132.23, 129.62, 129.28, 127.27, 124.83, 120.01, 116.95, 112.92; ESI (HRMS) (*m*/*z*) calcd for $C_{15}H_9BrClO_2$ $[M+H]^+$ 334.9474, found: 334.9470.

*4.3.14. 3-Bromo-4-(4-butoxyphenyl)-2H-chromen-2-one (**2.10**).* White solid (0.103 g, 74%); mp 132–134 °C, R_f (10% ethyl acetate in hexane) 0.46; IR (KBr, cm^{-1}): 2961, 1731, 1720, 1609, 1509, 1246, 1181, 1036, 990, 756; δ_H NMR (500 MHz, $CDCl_3$): 7.57–7.53 (m, 1H, Ar–H), 7.40 (d, *J*=8.55 Hz, 1H, Ar–H), 7.24–7.16 (m, 4H, Ar–H), 7.06 (d, *J*=9.15 Hz, 2H, Ar–H), 4.05 (t, *J*=6.4 Hz, 2H), 1.85–1.80 (m, 2H), 1.56–1.52 (m, 2H), 1.01 (t, *J*=7.32 Hz, 3H); δ_C NMR (125 MHz, $CDCl_3$): 159.92, 157.51, 154.57, 152.45, 131.91, 129.72, 127.75, 127.05, 124.60, 120.58, 116.81, 114.65, 112.75, 67.84, 31.27, 19.26, 13.85; ESI (HRMS) (*m*/*z*) calcd for $C_{19}H_{18}BrO_3$ $[M+H]^+$ 373.0439, found: 373.0435.

*4.3.15. 3-Bromo-4-(4-(trifluoromethyl)phenyl)-2H-chromen-2-one (**2.11**).* Light yellow solid (0.050 g, 36%); mp 132–134 °C, R_f (10% ethyl acetate in hexane) 0.48; IR (KBr, cm^{-1}): 1737, 1599, 1449, 1324, 1175, 1121, 1109, 1068, 998, 815, 753; δ_H NMR (400 MHz, $CDCl_3$): 7.85 (d, *J*=8.24 Hz, 2H, Ar–H), 7.61–7.57 (m, 1H, Ar–H), 7.46–7.42 (m, 3H, Ar–H), 7.21 (t, *J*=8.24 Hz, 1H, Ar–H), 6.99 (d, *J*=8.24 Hz, 1H, Ar–H); δ_C NMR (100 MHz, $CDCl_3$): 156.95, 153.11, 152.48, 138.80, 132.39, 131.57 (q, *J*=32.89 Hz), 128.72, 127.09, 126.06, 126.02, 124.93, 123.72 (q, *J*=273.68 Hz), 119.79, 117.05, 112.93; EI (HRMS) (*m*/*z*) calcd for $C_{16}H_8BrF_3O_2$ $[M]^+$ 367.9660, found: 367.9668.

*4.3.16. 3-Bromo-4-(4-methoxyphenyl)-6-phenyl-2H-chromen-2-one (**2.12**).* Light brown solid (0.119 g, 78%); mp 210–212 °C, R_f (10% ethyl acetate in hexane) 0.40; IR (KBr, cm^{-1}): 1724, 1606, 1508, 1245, 1180, 1026, 991, 830, 762, 699, 646; δ_H NMR (500 MHz, $CDCl_3$): 7.77 (dd, *J*=2.27, 8.57 Hz, 1H, Ar–H), 7.47 (d, *J*=8.6 Hz, 1H, Ar–H), 7.41–7.38 (m, 4H, Ar–H), 7.36–7.31 (m, 2H, Ar–H), 7.29 (d, *J*=8.6 Hz, 2H, Ar–H), 7.09 (d, *J*=8.6 Hz, 2H, Ar–H), 3.91 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 160.28, 157.45, 154.53, 151.83, 139.37, 138.06, 130.91, 129.75, 128.94, 127.78, 127.20, 127.07, 125.86, 120.74, 117.22, 114.28, 113.19, 55.37; ESI (HRMS) (*m*/*z*) calcd for $C_{22}H_{16}BrO_3$ $[M+H]^+$ 407.0283, found: 407.0287.

*4.3.17. 3-Bromo-6-phenyl-4-p-tolyl-2H-chromen-2-one (**2.13**).* Colorless solid (0.108 g, 74%); mp 186–188 °C, R_f (10% ethyl acetate in hexane) 0.48; IR (KBr, cm^{-1}): 1728, 1553, 1507, 1402, 1346, 1288, 1248, 1179, 1075, 986, 818, 759, 695, 629; δ_H NMR (500 MHz, $CDCl_3$): 7.76 (dd, *J*=2.02, 8.57 Hz, 1H, Ar–H), 7.47 (d, *J*=8.6 Hz, 1H, Ar–H), 7.41–7.33 (m, 7H, Ar–H), 7.28 (d, *J*=2 Hz, 1H, Ar–H), 7.23 (d, *J*=8.0 Hz, 2H, Ar–H), 2.48 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 157.40, 154.85, 151.83, 139.52, 139.39, 138.09, 132.16, 130.96, 129.60, 128.91, 128.02, 127.76, 127.10, 125.84, 120.62, 117.18, 113.00, 21.49; ESI (HRMS) (*m*/*z*) calcd for $C_{22}H_{16}BrO_2$ $[M+H]^+$ 391.0334, found: 391.0338.

*4.3.18. 3-Bromo-4-(4-ethoxyphenyl)-6-phenyl-2H-chromen-2-one (**2.14**).* Off white solid (0.128 g, 81%); mp166–168 °C, R_f (10% ethyl acetate in hexane) 0.0.44; IR (KBr, cm^{-1}): 1727, 1608, 1508, 1470, 1250, 1179, 983, 834, 760, 693, 610; δ_H NMR (500 MHz, $CDCl_3$): 7.77 (dd, *J*=2.3, 8.6 Hz, 1H, Ar–H), 7.47 (d, *J*=8.6 Hz, 1H, Ar–H), 7.41–7.38 (m, 4H, Ar–H), 7.35–7.32 (m, 2H, Ar–H), 7.27 (d, *J*=8.85 Hz, 2H, Ar–H), 7.07 (d, *J*=8.6 Hz, 2H, Ar–H), 4.13 (q, *J*=6.96 Hz, 2H), 1.48 (t, *J*=6.87 Hz, 3H); δ_C NMR (125 MHz, $CDCl_3$): 159.71, 157.46, 154.58, 151.82, 139.35, 138.02, 130.87, 129.73, 128.93, 127.76, 127.05, 126.99, 125.87, 120.74, 117.20, 114.68, 113.12, 63.60, 14.80; ESI (HRMS) (*m*/*z*) calcd for $C_{23}H_{18}BrO_3$ $[M+H]^+$ 421.0439, found: 421.0437.

*4.3.19. 3-Bromo-6-phenyl-4-m-tolyl-2H-chromen-2-one (**2.15**).* Off white solid (0.103 g, 70%); mp 120–122 °C, R_f (10% ethyl acetate in hexane) 0.52; IR (KBr, cm^{-1}): 1724, 1605, 1554, 1476, 1451, 1250,

990, 832, 766, 700; δ_H NMR (500 MHz, $CDCl_3$): 7.76 (dd, J=2.0, 8.6 Hz, 1H, Ar–H), 7.48–7.44 (m, 2H, Ar–H), 7.40–7.32 (m, 6H, Ar–H), 7.24 (d, J=2.3 Hz, 1H, Ar–H), 7.12 (d, J=7.45 Hz, 2H, Ar–H), 2.45 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 157.39, 154.93, 151.83, 139.37, 138.80, 138.09, 135.12, 130.98, 130.19, 128.93, 128.81, 128.46, 127.77, 127.08, 125.81, 125.01, 120.60, 117.18, 112.93, 21.54; ESI (HRMS) (m/z) calcd for $C_{22}H_{16}BrO_2$ $[M+H]^+$ 391.0334, found: 391.0331.

*4.3.20. 3-Bromo-4-(4-isopropoxyphenyl)-6-phenyl-2H-chromen-2-one (**2.16**).* White solid (0.129 g, 79%); mp148–150 °C, R_f (10% ethyl acetate in hexane) 0.46; IR (KBr, cm^{-1}): 1727, 1607, 1505, 1244, 1155, 992, 832, 762; δ_H NMR (500 MHz, $CDCl_3$): 7.76 (dd, J=2, 8.6 Hz, 1H, Ar–H), 7.47 (d, J=8.6 Hz, 1H, Ar–H), 7.41–7.40 (m, 4H, Ar–H), 7.35–7.34 (m, 2H, Ar–H), 7.27 (s, 2H, Ar–H), 7.05 (d, J=8.6 Hz, 2H, Ar–H), 4.69–4.62 (m, 1H), 1.41 (d, J=6.3 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 158.72, 157.50, 154.60, 151.82, 139.40, 138.03, 130.89, 129.81, 128.93, 127.76, 127.09, 126.74, 125.92, 120.73, 117.20, 115.71, 113.10, 70.05, 22.04; ESI (HRMS) (m/z) calcd for $C_{24}H_{20}BrO_3$ $[M+H]^+$ 435.0596, found: 435.0597.

*4.3.21. 3-Bromo-4-(4-fluorophenyl)-6-phenyl-2H-chromen-2-one (**2.17**).* White solid (0.089 g, 60%); mp 156–158 °C, R_f (10% ethyl acetate in hexane) 0.56; IR (KBr, cm^{-1}): 1734, 1604, 1505, 1224, 1003, 841, 761; δ_H NMR (500 MHz, $CDCl_3$): 7.78 (dd, J=2.3, 8.6 Hz, 1H, Ar–H), 7.49 (d, J=8.6 Hz, 1H, Ar–H), 7.41–7.38 (m, 4H, Ar–H), 7.36–7.33 (m, 3H, Ar–H), 7.30–7.26 (m, 2H, Ar–H), 7.20 (d, J=2.3 Hz, 1H, Ar–H); δ_C NMR (125 MHz, $CDCl_3$): 163.10 (d, J=248.36 Hz.), 157.16, 153.70, 151.79, 139.18, 138.24, 131.14, 130.22 (d, J=8.4 Hz), 128.99, 127.90, 127.02, 125.48, 120.41, 117.34, 116.29 (d, J=21.58 Hz), 113.51; ESI (HRMS) (m/z) calcd for $C_{21}H_{13}BrFO_2$ $[M+H]^+$ 395.0083, found: 395.0085.

*4.3.22. 3-Bromo-4-p-tolyl-2H-benzo[h]chromen-2-one (**2.18**).* Light yellow solid (0.099 g, 72%); mp 186–188 °C, R_f (10% ethyl acetate in hexane) 0.56; IR (KBr, cm^{-1}): 1725, 1510, 1349, 1272, 1053, 939, 766, 752; δ_H NMR (500 MHz, $CDCl_3$): 8.63–8.61 (m, 1H, Ar–H), 7.85–7.83 (m, 1H, Ar–H), 7.67–7.65 (m, 2H, Ar–H), 7.55 (d, J=9.15 Hz, 1H, Ar–H), 7.40 (d, J=7.9 Hz, 2H, Ar–H), 7.23 (d, J=7.9 Hz, 2H, Ar–H), 7.09 (d, J=9.15 Hz, 1H, Ar–H), 2.49 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 157.61, 155.69, 149.65, 139.40, 134.72, 132.73, 129.54, 129.03, 128.07, 127.72, 127.45, 124.48, 122.96, 122.81, 122.51, 115.69, 112.03, 21.47; ESI (HRMS) (m/z) calcd for $C_{20}H_{14}BrO_2$ $[M+H]^+$ 365.0177, found: 365.0174.

*4.3.23. 3-Bromo-4-phenyl-2H-benzo[h]chromen-2-one (**2.19**).* Light yellow solid (0.082 g, 62%); mp 174–176 °C, R_f (10% ethyl acetate in hexane) 0.58; IR (KBr, cm^{-1}): 1727, 1633, 1598, 1350, 1098, 1050, 936, 825, 756, 734, 700, 635; δ_H NMR (500 MHz, $CDCl_3$): 8.63–8.61 (m, 1H, Ar–H), 7.85–7.84 (m, 1H, Ar–H), 7.68–7.66 (m, 2H, Ar–H), 7.61–7.55 (m, 4H, Ar–H), 7.34 (d, J=6.7 Hz, 2H, Ar–H), 7.05 (d, J=8.55 Hz, 1H, Ar–H); δ_C NMR (125 MHz, $CDCl_3$): 157.56, 155.50, 149.69, 135.70, 134.73, 129.32, 129.08, 128.89, 128.09, 127.74, 127.49, 124.57, 122.83, 122.79, 122.49, 115.56, 112.03; ESI (HRMS) (m/z) calcd for $C_{19}H_{12}BrO_2$ $[M+H]^+$ 351.0021, found: 351.0027.

*4.3.24. 3-Bromo-4-(4-methoxyphenyl)-2H-benzo[h]chromen-2-one (**2.20**).* Yellow solid (0.101 g, 70%); mp 190–192 °C, R_f (10% ethyl acetate in hexane) 0.44; IR (KBr, cm^{-1}): 1724, 1607, 1510, 1291, 1250, 1177, 1028, 936, 836, 820, 760, 568; δ_H NMR (500 MHz, $CDCl_3$): 8.62–8.60 (m, 1H, Ar–H), 7.85–7.83 (m, 1H, Ar–H), 7.67–7.65 (m, 2H, Ar–H), 7.56 (d, J=9.15 Hz, 1H, Ar–H), 7.29–7.26 (m, 2H, Ar–H), 7.14–7.09 (m, 3H, Ar–H), 3.92 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 160.26, 157.64, 155.36, 149.61, 134.70, 130.10, 129.77, 129.01, 127.70, 127.44, 124.47, 122.97, 122.80, 122.50, 115.76, 114.23, 112.22, 55.38; ESI (HRMS) (m/z) calcd for $C_{20}H_{14}BrO_3$ $[M+H]^+$ 381.0126, found: 381.0123.

*4.3.25. 3-Bromo-4-(4-ethoxyphenyl)-2H-benzo[h]chromen-2-one (**2.21**).* Yellow solid (0.122 g, 82%); mp 170–172 °C, R_f (10% ethyl acetate in hexane) 0.50; IR (KBr, cm^{-1}): 1726, 1606, 1508, 1246, 1177, 1041, 822, 766; δ_H NMR (500 MHz, $CDCl_3$): 8.63–8.61 (m, 1H, Ar–H), 7.85–7.83 (m, 1H, Ar–H), 7.67–7.65 (m, 2H, Ar–H), 7.57 (d, J=8.55 Hz, 1H, Ar–H), 7.28–7.26 (m, 2H, Ar–H), 7.14 (d, J=8.55 Hz, 1H, Ar–H), 7.08 (d, J=9.2 Hz, 2H, Ar–H), 4.15 (q, J=6.91 Hz, 2H), 1.50 (t, J=7.0 Hz, 3H); δ_C NMR (125 MHz, $CDCl_3$): 159.69, 157.68, 155.44, 149.63, 134.71, 129.76, 129.01, 127.71, 127.54, 127.44, 124.46, 123.02, 122.83, 122.53, 115.80, 114.67, 112.20, 63.63, 14.81; ESI (HRMS) (m/z) calcd for $C_{21}H_{16}BrO_3$ $[M+H]^+$ 395.0283, found: 395.0288.

*4.3.26. 3-Bromo-4-(4-isopropoxyphenyl)-2H-benzo[h]chromen-2-one (**2.22**).* Light yellow solid (0.132 g, 86%); mp 168–170 °C, R_f (10% ethyl acetate in hexane) 0.54; IR (KBr, cm^{-1}): 1727, 1607, 1507, 1241, 1120, 1099, 821, 765; δ_H NMR (500 MHz, $CDCl_3$): 8.62–8.60 (m, 1H, Ar–H), 7.85–7.83 (m, 1H, Ar–H), 7.67–7.65 (m, 2H, Ar–H), 7.56 (d, J=9.15 Hz, 1H, Ar–H), 7.27–7.25 (m, 2H, Ar–H), 7.16 (d, J=9.15 Hz, 1H, Ar–H), 7.06 (d, J=9.15 Hz, 2H, Ar–H), 4.69–4.64 (m, 1H), 1.42 (d, J=6.1 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 158.71, 157.69, 155.45, 149.61, 134.70, 129.82, 128.99, 127.70, 127.41, 127.29, 124.43, 123.07, 122.83, 122.51, 115.80, 115.70, 112.16, 70.06, 22.06; ESI (HRMS) (m/z) calcd for $C_{22}H_{18}BrO_3$ $[M+H]^+$ 409.0439, found: 409.0439.

*4.3.27. 3,6-Dibromo-4-p-tolyl-2H-chromen-2-one (**2.23**).* White solid (0.106 g, 72%); mp 188–190 °C, R_f (10% ethyl acetate in hexane) 0.60; IR (KBr, cm^{-1}): 1721, 1593, 1545, 1466, 1398, 1262, 1246, 990, 819, 628; δ_H NMR (500 MHz, $CDCl_3$): 7.64 (dd, J=2.12, 8.82 Hz, 1H, Ar–H), 7.38 (d, J=7.9 Hz, 2H, Ar–H), 7.28 (d, J=8.55 Hz, 1H, Ar–H), 7.21 (d, J=2.45 Hz, 1H, Ar–H), 7.17 (d, J=8.55 Hz, 2H, Ar–H), 2.48 (s, 3H). δ_C NMR (125 MHz, $CDCl_3$): 156.79, 153.64, 151.31, 139.85, 134.75, 131.61, 129.87, 129.76, 127.93, 121.97, 118.55, 117.53, 113.95, 21.49; ESI (HRMS) (m/z) calcd for $C_{16}H_{11}Br_2O_2$ $[M+H]^+$ 394.9105, found: 394.9115.

*4.3.28. 3,6-Dibromo-4-(4-methoxyphenyl)-2H-chromen-2-one (**2.24**).* White solid (0.109 g, 71%); mp 158–160 °C, R_f (10% ethyl acetate in hexane) 0.52; IR (KBr, cm^{-1}): 1725, 1607, 1509, 1258, 1187, 1021, 993, 822; δ_H NMR (500 MHz, $CDCl_3$): 7.64 (dd, J=2.12, 8.82 Hz, 1H, Ar–H),7.29–7.22 (m, 4H, Ar–H), 7.09 (d, J=9.15 Hz, 2H, Ar–H), 3.91 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 160.50, 156.83, 153.32, 151.30, 134.73, 129.90, 129.66, 126.59, 122.08, 118.57, 117.52, 114.47, 114.12, 55.41; ESI (HRMS) (m/z) calcd for $C_{16}H_{11}Br_2O_3$ $[M+H]^+$ 410.9054, found: 410.9052.

*4.3.29. 3,6-Dibromo-4-(4-ethoxyphenyl)-2H-chromen-2-one (**2.25**).* White solid (0.118 g, 74%); mp 160–162 °C, R_f (10% ethyl acetate in hexane) 0.54; IR (KBr, cm^{-1}): 1724, 1608, 1509, 1474, 1251, 1179, 996, 828, 608; δ_H NMR (500 MHz, $CDCl_3$): 7.64 (dd, J=2.3, 8.6 Hz, 1H, Ar–H),7.29–7.26 (m, 2H, Ar–H), 7.21 (d, J=8.6 Hz, 2H, Ar–H), 7.07 (d, J=8.85 Hz, 2H, Ar–H), 4.14 (q, J=6.96 Hz, 2H), 1.48 (t, J=7.02 Hz, 3H); δ_C NMR (125 MHz, $CDCl_3$): 159.90, 156.88, 153.39, 151.26, 134.70, 129.92, 129.63, 126.34, 122.06, 118.55, 117.50, 114.84, 114.05, 63.65, 14.80; ESI (HRMS) (m/z) calcd for $C_{17}H_{13}Br_2O_3$ $[M+H]^+$ 424.9211, found: 424.9216.

*4.3.30. 3,6-Dibromo-4-(4-isopropoxyphenyl)-2H-chromen-2-one (**2.26**).* White solid (0.118 g, 72%); mp 136–138 °C, R_f (10% ethyl acetate in hexane) 0.54; IR (KBr, cm^{-1}): 1731, 1608, 1508, 1466, 1254, 1184, 992, 954, 818, 727; δ_H NMR (500 MHz, $CDCl_3$): 7.63 (dd, J=2.42, 8.72 Hz, 1H, Ar–H), 7.28–7.26 (m, 2H, Ar–H), 7.20 (d, J=8.9 Hz, 2H, Ar–H), 7.05 (d, J=8.6 Hz, 2H, Ar–H), 4.67–4.63 (m,

1H), 1.42 (d, J=6.0 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 158.93, 156.89, 153.40, 151.27, 134.69, 129.93, 129.69, 126.07, 122.06, 118.54, 117.49, 115.80, 114.01, 70.06, 22.04; ESI (HRMS) (m/z) calcd for $C_{18}H_{15}Br_2O_3$ $[M+H]^+$ 438.9367, found: 438.9381.

*4.3.31. 3,6,8-Tribromo-4-(4-methoxyphenyl)-2H-chromen-2-one (**2.27**).* White solid (0.112 g, 61%); mp 192–194 °C, R_f (10% ethyl acetate in hexane) 0.54; IR (KBr, cm^{-1}): 1735, 1608, 1535, 1506, 1436, 1321, 1296, 1246, 1178, 1165, 1004, 847, 786, 759, 651; δ_H NMR (400 MHz, $CDCl_3$): 7.90 (d, J=2.32 Hz, 1H, Ar–H), 7.22–7.19 (m, 3H, Ar–H), 7.09 (d, J=9.16 Hz, 2H, Ar–H), 3.91 (s, 3H); δ_C NMR (100 MHz, $CDCl_3$): 160.58, 155.87, 152.98, 148.36, 137.45, 129.60, 129.26, 126.33, 122.87, 117.30, 114.89, 114.53, 111.50, 55.41; ESI (HRMS) (m/z) calcd for $C_{16}H_{10}Br_3O_3$ $[M+H]^+$ 488.8160, found: 488.8161.

*4.3.32. 3,6,8-Tribromo-4-(4-isopropoxyphenyl)-2H-chromen-2-one (**2.28**).* Light yellow solid (0.129 g, 67%); mp 152–154 °C, R_f (10% ethyl acetate in hexane) 0.60; IR (KBr, cm^{-1}): 1730, 1606, 1504, 1433, 1247, 1170, 1015, 955, 840, 654; δ_H NMR (500 MHz, $CDCl_3$): 7.90 (d, J=1.85 Hz, 1H, Ar–H), 7.26–7.17 (m, 3H, Ar–H), 7.05 (d, J=8.55 Hz, 2H, Ar–H), 4.68–4.63 (m, 1H), 1.42 (d, J=6.15 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 159.04, 155.94, 153.06, 148.36, 137.43, 129.65, 129.31, 125.84, 122.88, 117.28, 115.87, 114.81, 111.48, 70.09, 22.02; ESI (HRMS) (m/z) calcd for $C_{18}H_{14}Br_3O_3$ $[M+H]^+$ 516.8473, found: 516.8472.

*4.3.33. 3,6,8-Tribromo-4-p-tolyl-2H-chromen-2-one (**2.29**).* White solid (0.120 g, 68%); mp 160–162 °C, R_f (10% ethyl acetate in hexane) 0.62; IR (KBr, cm^{-1}): 1732, 1538, 1505, 1431, 1250, 1009, 862, 844, 813, 738, 723, 651, 605, 507; δ_H NMR (500 MHz, $CDCl_3$): 7.90 (d, J=2.45 Hz, 1H, Ar–H), 7.38 (d, J=7.9 Hz, 2H, Ar–H), 7.16–7.14 (m, 3H, Ar–H), 2.48 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 155.86, 153.29, 148.37, 140.05, 137.48, 131.37, 129.85, 129.22, 127.84, 122.75, 117.32, 114.74, 111.49, 21.51; ESI (HRMS) (m/z) calcd for $C_{16}H_{10}Br_3O_2$$[M+H]^+$ 472.8210, found: 472.8213.

*4.3.34. 3,4-Bis (4-methoxyphenyl)-2H-chromen-2-one (**3.1**).*[6a] White solid (0.108 g, 80%); mp 172–174 °C, R_f (10% ethyl acetate in hexane) 0.20; IR (KBr, cm^{-1}): 1709, 1610, 1592, 1507, 1448, 1291, 1244, 1175, 1159, 1033, 980, 809, 767, 622; δ_H NMR (400 MHz, $CDCl_3$): 7.53–7.49 (m, 1H, Ar–H), 7.41 (d, J=8.24 Hz, 1H, Ar–H), 7.28 (dd, J=1.36, 8.24 Hz, 1H, Ar–H), 7.20–7.15 (m, 1H, Ar–H), 7.07–7.03 (m, 4H, Ar–H), 6.84 (d, J=9.16 Hz, 2H, Ar–H), 6.74 (d, J=8.72 Hz, 2H, Ar–H), 3.80 (s, 3H), 3.75 (s, 3H); δ_C NMR (100 MHz, $CDCl_3$): 161.62, 159.34, 158.73, 153.08, 150.87, 131.87, 131.11, 130.84, 127.69, 126.78, 126.49, 126.28, 123.98, 120.82, 116.69, 113.76, 113.29, 55.20, 55.11; ESI (HRMS) (m/z) calcd for $C_{23}H_{19}O_4$ $[M+H]^+$ 359.1283, found: 359.1280.

*4.3.35. 3-(4-Isopropoxyphenyl)-4-(4-methoxyphenyl)-2H-chro-men-2-one (**3.2**).* White solid (0.105 g, 72%); mp 112–114 °C, R_f (10% ethyl acetate in hexane) 0.30; IR (KBr, cm^{-1}): 1720, 1608, 1505, 1446, 1296, 1249, 1176, 1113, 982, 950, 819, 762, 572; δ_H NMR (500 MHz, $CDCl_3$): 7.52–7.49 (m, 1H, Ar–H), 7.41 (d, J=8.2 Hz, 1H, Ar–H), 7.29–7.27 (m, 1H, Ar–H), 7.19–7.16 (m, 1H, Ar–H), 7.05–7.02 (m, 4H, Ar–H), 6.85–6.83 (m, 2H, Ar–H), 6.71–6.70 (m, 2H, Ar–H), 4.51–4.46 (m, 1H), 3.80 (s, 3H), 1.29 (d, J=5.8 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 161.65, 159.33, 157.12, 153.07, 150.82, 131.91, 131.07, 130.86, 127.69, 126.84, 126.55, 125.98, 123.96, 120.87, 116.69, 115.06, 113.75, 69.73, 55.21, 22.02; ESI (HRMS) (m/z) calcd for $C_{25}H_{23}O_4$ $[M+H]^+$ 387.1596, found: 387.1594.

*4.3.36. 4-(4-Ethoxyphenyl)-3-(4-methoxyphenyl)-2H-chromen-2-one (**3.3**).* White solid (0.104 g, 75%); mp 150–152 °C, R_f (10% ethyl acetate in hexane) 0.28; IR (KBr, cm^{-1}): 1705, 1609, 1507, 1449, 1290, 1246, 1175, 1160, 980, 819, 766; δ_H NMR (500 MHz, $CDCl_3$): 7.52–7.49 (m, 1H, Ar–H), 7.40 (d, J=7.95 Hz, 1H, Ar–H), 7.29 (dd, J=1.22, 7.92 Hz, 1H, Ar–H), 7.19–7.16 (m, 1H, Ar–H), 7.07–7.02 (m, 4H, Ar–H), 6.83 (d, J=9.15 Hz, 2H, Ar–H), 6.74 (d, J=8.55 Hz, 2H, Ar–H), 4.02 (q, J=6.91 Hz, 2H), 3.75 (s, 3H), 1.41 (t, J=7.02 Hz, 3H); δ_C NMR (125 MHz, $CDCl_3$): 161.65, 158.74, 158.71, 153.06, 150.94, 131.87, 131.10, 130.82, 127.71, 126.59, 126.42, 126.28, 123.97, 120.82, 116.67, 114.22, 113.27, 63.40, 55.10, 14.76; ESI (HRMS) (m/z) calcd for $C_{24}H_{21}O_4$ $[M+H]^+$ 373.1440, found: 373.1443.

*4.3.37. 3,4-Bis(4-ethoxyphenyl)-2H-chromen-2-one (**3.4**).* White solid (0.110 g, 76%); mp 100–102 °C, R_f (10% ethyl acetate in hexane) 0.26; IR (KBr, cm^{-1}): 1714, 1610, 1508, 1450, 1289, 1246, 1172, 1162, 1112, 1045, 983, 820, 764, 561; δ_H NMR (400 MHz, $CDCl_3$): 7.52–7.48 (m, 1H, Ar–H), 7.40 (d, J=7.36 Hz, 1H, Ar–H), 7.29 (dd, J=1.4, 8.24 Hz, 1H, Ar–H), 7.19–7.15 (m, 1H, Ar–H), 7.05–7.01 (m, 4H, Ar–H), 6.83 (d, J=8.72 Hz, 2H, Ar–H), 6.72 (d, J=9.16 Hz, 2H, Ar–H), 4.04–3.94 (m, 4H), 1.43–1.35 (m, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.61, 158.77, 158.17, 153.11, 150.88, 131.88, 131.06, 130.85, 127.71, 126.69, 126.54, 126.17, 123.94, 120.89, 116.68, 114.26, 113.81, 63.42, 63.28, 14.78; ESI (HRMS) (m/z) calcd for $C_{25}H_{23}O_4$ $[M+H]^+$ 387.1596, found: 387.1596.

*4.3.38. 4-(4-Isopropoxyphenyl)-3-phenyl-2H-chromen-2-one (**3.5**).* White solid (0.098 g, 73%); mp 138–140 °C, R_f (10% ethyl acetate in hexane) 0.34; IR (KBr, cm^{-1}): 1707, 1604, 1508, 1448, 1242, 1117, 951, 772, 697; δ_H NMR (500 MHz, $CDCl_3$): 7.54–7.51 (m, 1H, Ar–H), 7.42 (d, J=8.55 Hz, 1H, Ar–H), 7.33 (d, J=7.95 Hz, 1H, Ar–H), 7.20–7.17 (m, 4H, Ar–H), 7.13 (d, J=6.7 Hz, 2H, Ar–H), 7.01 (d, J=8.55 Hz, 2H, Ar–H), 6.80 (d, J=8.55 Hz, 2H, Ar–H), 4.54–4.49 (m, 1H), 1.32 (d, J=5.5 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 161.40, 157.79, 153.21, 151.48, 134.13, 131.30, 130.85, 130.57, 127.88, 127.74, 127.46, 126.77, 126.18, 124.01, 120.71, 116.72, 115.41, 69.85, 21.92; ESI (HRMS) (m/z) calcd for $C_{24}H_{21}O_3$ $[M+H]^+$ 357.1491, found: 357.1490.

*4.3.39. 4-(4-Isopropoxyphenyl)-3-(4-methoxyphenyl)-2H-chromen-2-one (**3.6**).* White solid (0.102 g, 70%); mp 132–134 °C, R_f (10% ethyl acetate in hexane) 0.60; IR (KBr, cm^{-1}): 2978, 1708, 1611, 1594, 1507, 1449, 1287, 1244, 1159, 981, 813, 768, 637, 594; δ_H NMR (500 MHz, $CDCl_3$): 7.52–7.48 (m, 1H, Ar–H), 7.40 (d, J=8.55 Hz, 1H, Ar–H), 7.31 (dd, J=1.82, 7.92 Hz, 1H, Ar–H), 7.19–7.16 (m, 1H, Ar–H), 7.06 (d, J=9.15 Hz, 2H, Ar–H), 7.01 (d, J=9.15 Hz, 2H, Ar–H) 6.82 (d, J=8.55 Hz, 2H, Ar–H), 6.74 (d, J=8.55 Hz, 2H, Ar–H), 4.56–4.51 (m, 1H), 3.75 (s, 3H), 1.34 (d, J=6.15 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.65, 158.74, 157.75, 153.10, 150.96, 131.90, 131.10, 130.88, 127.76, 126.49, 126.41, 126.34, 123.96, 120.84, 116.68, 115.53, 113.27, 69.91, 55.12, 21.97; ESI (HRMS) (m/z) calcd for $C_{25}H_{23}O_4$ $[M+H]^+$ 387.1596, found: 387.1592.

*4.3.40. 3,4-Bis(4-isopropoxyphenyl)-2H-chromen-2-one (**3.7**).* White solid (0.114 g, 72%); mp 116–118 °C, R_f (10% ethyl acetate in hexane) 0.32; IR (KBr, cm^{-1}): 1706, 1606, 1506, 1450, 1290, 1248, 1181, 1135, 986, 952, 863, 835, 769; δ_H NMR (500 MHz, $CDCl_3$): 7.52–7.48 (m, 1H, Ar–H), 7.40 (d, J=8.55 Hz, 1H, Ar–H), 7.31 (d, J=7.95 Hz, 1H, Ar–H), 7.19–7.16 (m, 1H, Ar–H), 7.04–7.00 (m, 4H, Ar–H), 6.81 (d, J=8.55 Hz, 2H, Ar–H), 6.70 (d, J=8.55 Hz, 2H, Ar–H), 4.56–4.45 (m, 2H), 1.33 (d, J=6.1 Hz, 6H), 1.29 (d, J=6.1 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.66, 157.71, 157.10, 153.06, 150.89, 131.92, 131.04, 130.89, 127.74, 126.52, 126.45, 126.03, 123.93, 120.85, 116.65, 115.49, 115.04, 69.88, 69.72, 22.00, 21.95; ESI (HRMS) (m/z) calcd for $C_{27}H_{27}O_4$ $[M+H]^+$ 415.1909, found: 415.1905.

*4.3.41. 4-(4-Isopropoxyphenyl)-3-(4-methoxyphenyl)-6-phenyl-2H-chromen-2-one (**3.8**).* White solid (0.126 g, 73%); mp 156–158 °C, R_f (10% ethyl acetate in hexane) 0.21; IR (KBr, cm^{-1}): 2978, 1718, 1608,

1507, 1288, 1246, 1185, 1176, 1120, 980, 839, 834, 761, 695; δ_H NMR (500 MHz, $CDCl_3$): 7.73 (dd, J=1.85, 8.55 Hz, 1H, Ar–H), 7.50–7.33 (m, 7H, Ar–H), 7.06 (t, J=8.87 Hz, 4H, Ar–H), 6.83 (d, J=8.55 Hz, 2H, Ar–H), 6.75 (d, J=9.15 Hz, 2H, Ar–H), 4.56–4.51 (m, 1H), 3.76 (s, 3H), 1.33 (d, J=6.15 Hz, 6H); δ_C NMR (125 MHz, $CDCl_3$): 161.59, 158.76, 157.78, 152.54, 150.98, 139.90, 137.30, 131.91, 130.92, 130.08, 128.88, 127.51, 127.07, 126.70, 126.36, 126.02, 121.00, 117.09, 115.60, 113.27, 69.93, 55.13, 21.97; ESI (HRMS) (m/z) calcd for $C_{31}H_{26}NaO_4$ $[M+Na]^+$ 485.1729, found: 485.1720.

*4.3.42. 3,4-Bis(4-isopropoxyphenyl)-6-phenyl-2H-chromen-2-one (**3.9**).* White solid (0.136 g, 74%); mp 196–198 °C, R_f (10% ethyl acetate in hexane) 0.28; IR (KBr, cm^{-1}): 2979, 1713, 1606, 1507, 1477, 1300, 1242, 1181, 1122, 989, 952, 845, 823, 766, 701; δ_H NMR (400 MHz, $CDCl_3$): 7.74–7.71 (m, 1H, Ar–H), 7.51–7.33 (m, 7H, Ar–H), 7.05 (dd, J=2.28, 8.68 Hz, 4H, Ar–H), 6.83 (d, J=8.72 Hz, 2H, Ar–H), 6.72 (d, J=8.72 Hz, 2H, Ar–H), 4.57–4.47 (m, 2H), 1.33 (d, J=5.96 Hz, 6H), 1.30 (d, J=5.96 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.58, 157.80, 157.17, 152.56, 150.93, 139.95, 137.30, 131.95, 130.94, 130.02, 128.88, 127.51, 127.08, 126.80, 126.46, 126.08, 126.01, 121.05, 117.08, 115.63, 115.11, 69.95, 69.79, 22.01, 21.97; ESI (HRMS) (m/z) calcd for $C_{33}H_{31}O_4$ $[M+H]^+$ 491.2222, found: 491.2226.

*4.3.43. 3-(4-Ethoxyphenyl)-4-(4-isopropoxyphenyl)-2H benzo[h]-chromen-2-one (**3.10**).* Yellow solid (0.103 g, 61%); mp 164–166 °C, R_f (10% ethyl acetate in hexane) 0.26; IR (KBr, cm^{-1}): 2978, 1710, 1608, 1508, 1286, 1246, 1173, 1118, 1047, 823; δ_H NMR (500 MHz, $CDCl_3$): 8.67 (d, J=7.35 Hz, 1H, Ar–H), 7.85 (d, J=6.7 Hz, 1H, Ar–H), 7.66–7.62 (m, 2H, Ar–H), 7.57 (d, J=8.55 Hz, 1H, Ar–H), 7.31 (d, J=8.55 Hz, 1H, Ar–H), 7.09 (d, J=9.15 Hz, 2H, Ar–H), 7.05 (d, J=8.55 Hz, 2H, Ar–H), 6.84 (d, J=8.55 Hz, 2H, Ar–H), 6.74 (d, J=8.55 Hz, 2H, Ar–H), 4.58–4.53 (m, 1H), 3.98 (q, J=6.91 Hz, 2H), 1.39–1.34 (m, 9H); δ_C NMR (125 MHz, $CDCl_3$): 161.67, 158.11, 157.71, 151.84, 150.03, 134.40, 131.95, 130.95, 128.45, 127.57, 126.99, 126.91, 126.30, 125.99, 123.61, 123.41, 123.10, 122.67, 115.98, 115.54, 113.80, 69.90, 63.28, 21.98, 14.81; ESI (HRMS) (m/z) calcd for $C_{30}H_{27}O_4$ $[M+H]^+$ 451.1909, found: 451.1904.

*4.3.44. 3,4-Bis(4-isopropoxyphenyl)-2H-benzo[h]chromen-2-one (**3.11**).* Yellow solid (0.132 g, 76%); mp 124–126 °C, R_f (10% ethyl acetate in hexane) 0.28; IR (KBr, cm^{-1}): 2976, 1711, 1606, 1509, 1381, 1242, 1119, 1049, 953, 937, 832, 805, 535; δ_H NMR (400 MHz, $CDCl_3$): 8.67 (d, J=9.16 Hz, 1H, Ar–H), 7.86–7.84 (m, 1H, Ar–H), 7.67–7.61 (m, 2H, Ar–H), 7.56 (d, J=9.16 Hz, 1H, Ar–H), 7.31 (d, J=8.72 Hz, 1H, Ar–H), 7.09–7.04 (m, 4H, Ar–H), 6.84 (d, J=8.68 Hz, 2H, Ar–H), 6.73 (d, J=9.16 Hz, 2H, Ar–H), 4.58–4.46 (m, 2H, Ar–H), 1.35 (d, J=5.96 Hz, 6H), 1.31 (d, J=5.92 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.66, 157.72, 157.11, 151.82, 150.02, 134.40, 131.99, 130.96, 128.44, 127.57, 126.98, 126.19, 126.01, 123.60, 123.41, 123.10, 122.66, 116.00, 115.56, 115.08, 69.92, 69.75, 22.03, 21.98; ESI (HRMS) (m/z) calcd for $C_{31}H_{29}O_4$ $[M+H]^+$ 465.2066, found: 465.2060.

*4.3.45. 4-(4-Isopropoxyphenyl)-3-(4-methoxyphenyl)-2H-benzo-[h] chromen-2-one (**3.12**).* Light yellow solid (0.108 g, 66%); mp 182–184 °C, R_f (10% ethyl acetate in hexane) 0.24; IR (KBr, cm^{-1}): 1712, 1609, 1553, 1508, 1352, 1285, 1244, 1120, 1021, 824, 777, 749; δ_H NMR (400 MHz, $CDCl_3$): 8.68–8.66 (m, 1H, Ar–H), 7.86–7.84 (m, 1H, Ar–H), 7.67–7.61 (m, 2H, Ar–H), 7.57 (d, J=8.68 Hz, 1H, Ar–H), 7.31 (d, J=9.12 Hz, 1H, Ar–H), 7.11 (d, J=8.72 Hz, 2H, Ar–H), 7.05 (d, J=9.12 Hz, 2H, Ar–H), 6.85 (d, J=9.16 Hz, 2H, Ar–H), 6.76 (d, J=8.72 Hz, 2H, Ar–H), 4.59–4.52 (m, 1H), 3.76 (s, 3H), 1.35 (d, J=6.4 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.64, 158.72, 157.74, 151.87, 150.04, 134.42, 131.96, 130.94, 128.47, 127.58, 126.99, 126.90, 126.49, 125.94, 123.62, 123.40, 123.10, 122.66, 115.97, 115.57, 113.29, 69.94, 55.12, 21.98; ESI (HRMS) (m/z) calcd for $C_{29}H_{25}O_4$ $[M+H]^+$ 437.1753, found: 437.1759.

*4.3.46. 3-Bromo-6-(4-isopropoxyphenyl)-4-(4-methoxyphenyl)-2H-chromen-2-one (**4.1**).* White solid (0.105 g, 60%); mp 152–154 °C, R_f (10% ethyl acetate in hexane) 0.38; IR (KBr, cm^{-1}): 1721, 1607, 1505, 1472, 1275, 1246, 1184, 1120, 1029, 983, 827; δ_H NMR (400 MHz, $CDCl_3$): 7.59 (dd, J=2.28, 8.72 Hz, 1H, Ar–H), 7.38 (d, J=2.28 Hz, 1H, Ar–H), 7.28 (d, J=8.68 Hz, 1H, Ar–H), 7.02 (dd, J=2.06, 8.94 Hz, 4H, Ar–H), 6.86 (d, J=8.72 Hz, 2H, Ar–H), 6.71 (d, J=8.92 Hz, 2H, Ar–H), 4.51–4.45 (m, 1H), 3.81 (s, 3H), 1.29 (d, J=5.96 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 160.98, 159.55, 157.32, 151.90, 149.57, 133.82, 131.85, 130.76, 129.94, 127.51, 126.10, 125.47, 122.60, 118.42, 116.80, 115.06, 114.02, 69.73, 55.23, 22.00; ESI (HRMS) (m/z) calcd for $C_{25}H_{22}$ BrO_4 $[M+H]^+$ 465.0701, found: 465.0705.

*4.3.47. 3-(4-Ethoxyphenyl)-6-(4-isopropoxyphenyl)-4-(4-meth-oxy-phenyl)-2H-chromen-2-one (**4.2**).* White solid (0.061 g, 65%); mp 142–144 °C, R_f (10% ethyl acetate in hexane) 0.36; IR (KBr, cm^{-1}): 1709, 1608, 1517, 1505, 1477, 1246, 1182, 1126, 821; δ_H NMR (400 MHz, $CDCl_3$): 7.68 (dd, J=2.06, 8.46 Hz, 1H, Ar–H), 7.46–7.34 (m, 4H, Ar–H), 7.08–7.03 (m, 4H, Ar–H), 6.91 (d, J=8.72 Hz, 2H, Ar–H), 6.85 (d, J=8.68 Hz, 2H, Ar–H), 6.71 (d, J=8.68 Hz, 2H, Ar–H), 4.52–4.46 (m, 1H), 4.04 (q, J=7.01 Hz, 2H), 3.81 (s, 3H), 1.42 (t, J=7.1 Hz, 3H), 1.30 (d, J=5.96 Hz, 6H); δ_C NMR (100 MHz, $CDCl_3$): 161.65, 159.34, 158.68, 157.12, 152.11, 150.91, 137.00, 132.20, 131.93, 130.88, 129.68, 128.05, 126.80, 126.05, 125.33, 120.99, 116.99, 115.08, 114.86, 113.81 69.74, 63.53, 55.20, 22.03, 14.80; ESI (HRMS) (m/z) calcd for $C_{33}H_{31}O_5$ $[M+H]^+$ 507.2171, found: 507.2173.

*4.3.48. 3-Chloro-4-(4-methoxyphenyl)-2H-chromen-2-one (**5.1**).* White solid (0.042 g, 39%); mp 138–140 °C, R_f (10% ethyl acetate in hexane) 0.30; IR (KBr, cm^{-1}): 1729, 1607, 1507, 1349, 1247, 1175, 1040, 1015, 828, 764; δ_H NMR (400 MHz, $CDCl_3$): 7.55–7.51 (m, 1H, Ar–H), 7.40 (d, J=8.72 Hz, 1H, Ar–H), 7.29–7.27 (m, 2H, Ar–H), 7.23–7.18 (m, 2H, Ar–H), 7.09–7.07 (m, 2H, Ar–H), 3.90 (s, 3H); δ_C NMR (125 MHz, $CDCl_3$): 160.36, 157.58, 151.96, 150.96, 131.70, 130.05, 127.50, 125.05, 124.64, 120.54, 120.32, 116.85, 114.21, 55.37; EI (HRMS) (m/z) calcd for $C_{16}H_{11}ClO_3$ $[M]^+$ 286.0397, found: 286.0397.

Acknowledgements

The financial support received from the Council of Scientific and Industrial Research (CSIR), New Delhi (No. 02(0091)/12/EMR-II) is gratefully acknowledged. A. K also acknowledges the research fellowship received from the CSIR, New Delhi.

Supplementary data

Supplementary data (Supplementary data comprising ^1H and ^{13}C NMR and HRMS for all the products was given and it can be found in the online version.) related to this article can be found at http://dx.doi.org/10.1016/j.tet.2015.05.060.

References and notes

1. Garazd, M. M.; Garazd, Y. L.; Khilya, V. P. *Chem. Nat. Compd.* **2003**, *39*, 54–121.
2. (a) Stanley, S. A.; Kawate, T.; Iwase, N.; Shimizu, M.; Clatworthy, A. E.; Kazyanskaya, E.; Sacchettini, J. C.; Ioerger, T. R.; Siddiqi, N. A.; Minami, S.; Aquadro, J. A.; Grant, S. S.; Rubin, E. J.; Hung, D. T. *Proc. Natl. Acad. Sci. U.S.A.* **2013**, *110*, 11565–11570; (b) Pierson, J.-T.; Dume'tre, A.; Hutter, S.; Delmas, F.; Laget, M.; Finet, J.-P.; Azas, N.; Combes, S. *Eur. J. Med. Chem.* **2010**, *45*, 864–869; (c) Taechowisan, T.; Lu, C.; Shen, Y.; Lumyong, S. *Nat. Prod. Res.* **2007**, *21*, 1104–1113; (d) Taechowisan, H.; Lu, H.; Shen, Y.; Lumyong, A. *J. Cancer Res. Ther.* **2007**, *3*, 86–91.
3. (a) Sekino, E.; Kumamoto, T.; Tanaka, T.; Ikeda, T.; Ishikawa, T. *J. Org. Chem.* **2004**, *69*, 2760–2767; (b) Barancelli, D. A.; Salles, A. G., Jr.; Taylor, J. G.; Correia,

C. R. D. *Org. Lett.* **2012**, *14*, 6036–6039; (c) Gallagher, B. D.; Taft, B. R.; Lipshutz, B. H. *Org. Lett.* **2009**, *11*, 5374–5377.
4. Schiedel, M. S.; Briehn, C. A.; Bauerle, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 4677–4680.
5. (a) Shah, P.; Santana, M. D.; García, J.; Serrano, J. L.; Naik, M.; Pednekar, S.; Kapdi, A. R. *Tetrahedron* **2013**, *69*, 1446–1453; (b) Min, M.; Hong, S. *Chem. Commun.* **2012**, 9613–9615; (c) Wu, J.; Liao, Y.; Yang, Z. *J. Org. Chem.* **2001**, *66*, 3642–3645; (d) Schio, L.; Chatreaux, F.; Klich, M. *Tetrahedron Lett.* **2000**, *41*, 1543–1547; (e) Gao, W.; Luo, Y.; Ding, Q.; Peng, Y.; Wu, J. *Tetrahedron Lett.* **2010**, *51*, 136–138.
6. (a) Zhang, L.; Meng, T.; Fan, R.; Wu, J. *J. Org. Chem.* **2007**, *72*, 7279–7286; (b) Nakai, K.; Kurahashi, T.; Matsubara, S. *J. Am. Chem. Soc.* **2011**, *133*, 11066–11068; (c) Kadnikov, D. V.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3643–3646; (d) Kadnikov, D. V.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 9423–9432; (e) Hwang, I. T.; Lee, S. A.; Hwang, J. S.; Lee, K. I. *Molecules* **2011**, *16*, 6313–6321.
7. Rao, M. L. N.; Venkatesh, V.; Jadhav, D. N. *Eur. J. Org. Chem.* **2010**, 3945–3955.
8. Rao, M. L. N.; Kumar, A. *Tetrahedron* **2014**, *70*, 6995–7005.
9. Das, B.; Venkateswarlu, K.; Majhi, A.; Siddaiah, V.; Reddy, K. R. *J. Mol. Catal. A: Chem.* **2007**, *267*, 30–33.
10. (a) Audisio, D.; Messaoudi, S.; Peyrat, J.-F.; Brion, J.-D.; Alami, M. *Tetrahedron Lett.* **2007**, *48*, 6928–6932; (b) Soussi, M. A.; Audisio, D.; Messaoudi, S.; Provot, O.; Brion, J.-D.; Alami, M. *Eur. J. Org. Chem.* **2011**, 5077–5088.
11. (a) Tan, G.; Yao, Y.; Gu, Y.; Li, S.; Lv, M.; Wang, K.; Chen, H.; Li, X. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 2825–2830; (b) Chen, H.; Li, S.; Yao, Y.; Zhou, L.; Zhao, J.; Gu, Y.; Wang, K.; Li, X. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 4785–4789.
12. McKie, J. A.; Bhagwat, S. S.; Brady, H.; Doubleday, M.; Gayo, L.; Hickman, M.; Jalluri, R. K.; Khammung-khune, S.; Kois, A.; Mortensen, D.; Richard, N.; Sapienza, J.; Shevlin, G.; Stein, B.; Sutherland, M. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3407–3410.
13. Bury, P. S.; Christiansen, L. B.; Jacobsen, P.; Jørgensen, A. S.; Kanstrup, A.; Narum, L.; Bain, S.; Fledelius, C.; Gissel, B.; Hansen, B. S.; Korsgaard, N.; Thorpe, S. M.; Wassermann, K. *Bioorg. Med. Chem.* **2002**, *10*, 125–145.
14. *Organobismuth Chemistry*; Suzuki, H., Matano, Y., Eds.; Elsevier: Amsterdam, Netherlands, 2001.