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Synthesis of arylated coumarins by Suzuki-Miyaura cross-coupling. Reactions and anti-HIV activity

Aws M. Hamdy,[a,b] Zien Khaddour,[a] Najim A. Al-Masoudi,[c] Qamar Rahman,[a,d] Christian Hering-Junghans,[a] Alexander Villinger,[a] Peter Langer*,[a,e]

Abstract: Arylated coumarins were prepared by site-selective Suzuki-Miyauara cross-coupling reaction of the bis(triflate) of 4-methyl-6,7-dihydroxycoumarin. Triarylated coumarins were prepared by Suzuki-Miyauara cross-coupling reactions of 3-bromo-4-methyl-2-oxo-2*H*-chromene-6,7-diylbis(trifluoromethanesulfonate). The *in vitro* anti-HIV activity of the products was investigated. Two lead structures with considerable activities were identified.

Key words: Anti-HIV activity, Coumarins, Regioselective synthesis, Suzuki-Miyaura cross-coupling reaction

1. Introduction

Coumarin and its derivatives are one of the important classes of heterocyclic compounds which occur in many natural products with pharmacological activity.[1-6] For example, wedelolactone **1**, isolated from *Eclipta Elba*, and ellagic acid **2** show a broad range of biological activities,[7-10] while other coumestans were isolated from the roots of *Hedysarum multijugum*,[11] and exhibited anti-HCV activity.[12] Coumarin compounds are known to possess a wide range of biological activities, such as antibacterial,[13] anticancer,[14,15] anticoagulant,[16] anti-HIV protease inhibitory,[17] anti-HIV integrase,[18,19] and serine protease inhibitory activity.[20] They are inhibitors of steroid 5α-reductase,[21] and of NO synthase inhibitors.[22] Geiparvarin **3**, a naturally occurring product bearing the coumarin

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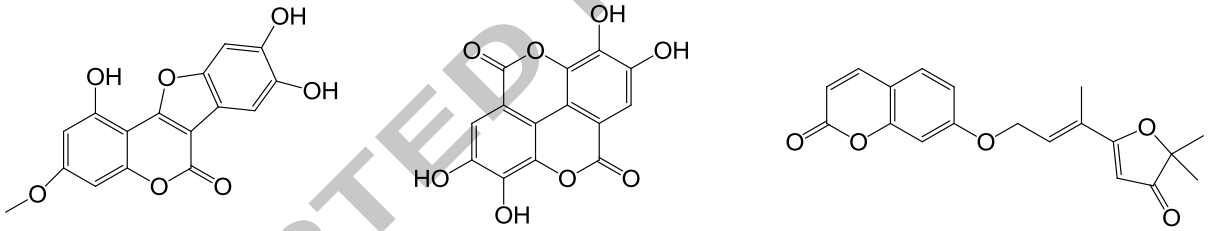
residue, has been shown to possess a significant inhibitory activity against a variety of cell lines including sarcoma 180, *Lewis* lung carcinoma, P-388 lymphocytic leukaemia, and *Walker* 256 carcinosarcoma.[23] New furanocoumarines, such as japonagelol, have been prepared as novel antiproliferative agents.[24] In addition, coumarins are widely used as additives in food chemicals, perfumes, agrochemicals, cosmetics, and dispersed fluorescent and laser dyes.[1,25-27]

Coumarins can be synthesized by various methods, such as Pechmann,[28] Perkin,[29] Knoevenagel,[30] and Wittig[31] reactions. Palladium-catalyzed site-selective cross-coupling reactions of 3-bromo-4-trifluormethylsulfonyloxycoumarin or 3-bromo-4-tosyloxycoumarin provide an efficient and facile route for the synthesis of 3,4-disubstituted coumarins.[32,33] However, some recent reviews[34,35] have been reported covering scope and limitations as well as a range of previous applications of the coupling reactions. Recently, we reported the synthesis of arylated coumarins by site-selective Suzuki–Miyaura cross-coupling reactions of the bis(triflate) of 4-methyl-6,7-dihydroxycoumarin.[36] Herein, we report full details of these studies. In addition to our short communication, we herein report, for the first time, the synthesis of a series of triarylated coumarins starting from 3-bromo-4-methyl-6,7-dihydroxycoumarin. In addition, the anti-HIV activity of a series of products has been investigated.



1. Wedelolactone **2**. Ellagic acid **3**. Geiparvarine

Figure 1. Natural occurring coumarins

2. Result and Discussion

2.1. Synthesis

4-Methyl-6,7-dihydroxycoumarin **(4)** has been selected as a key intermediate for the synthesis of new coumarin analogues. Thus, treatment of **4** with triflic anhydride (2.4 equiv) in the presence of Et_3N (4.0 equiv) at -78 ^oC afforded the bis(triflate) **5** in 75% yield (Scheme 1). Reaction of **5** with arylboronic acids **6** (2.2 equiv.) *via* Suzuki-Miyaura reaction gave 4-methyl-6,7-diarylcoumarines **7a-e** in 70-88% yield (Scheme 2). Both electron-poor and electron-rich arylboronic acids could be successfully employed. The best yields were obtained by using $Pd(PPh_3)_4$ (6 mol-%) as a catalyst and K_3PO_4 (3.0 equiv) as a base in dioxane at 120 °C for 6 h (Scheme 2, Table 1).

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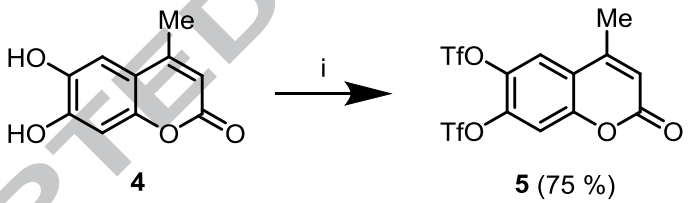
The structures of **5** and **7a-e** were assigned on the basis of their ^{1}H and ^{13}C NMR and mass spectra. In the ^{1}H NMR spectra, H-3 of the coumarin ring appeared in the regions δ 6.37- 6.22 ppm as a doublet ($J_{CH3,H3}$ ~ 1.2 Hz), while methyl groups at C-4 resonated in the region δ 2.41-2.38 ppm as a doublet as well. H-5 and H-8 protons appeared as broad singlets in the regions δ 7.53-7.41 and δ 7.59-7.27 ppm, respectively. The other protons of aromatic, methoxy and other methyl groups were fully analyzed (*cf.* Experimental section). The ^{13}C NMR spectra of **5** and **7a-e** contained similar resonance signals of the coumarin carbons ring C-2 - C-8a. The higher-field signals between δ_C 160.9 and 158.2 ppm were assigned to the carbonyl group of the benzopyran ring (C-2), while the resonances in the regions of δ_C 115.1-112.4 ppm were assigned to C-3. The chemical shifts in the regions δ_C 154.4-151.4 and 152.5-150.5 ppm were attributed to C-4 and C-8a, respectively. The resonances at δ_C 141.7-137.1 and δ_C 118.5-110.9 ppm were assigned to the coumarin carbons C-7 and C-8, respectively. The C-4a carbon atom appeared between δ_C 120.1 and 117.6 ppm, except for **5**, which resonated at δ_C 112.7 ppm. The resonances at the regions δ_C 126.4-125.1 ppm were attributed to C-5, C-6 and carbons of the aromatic ring, whereas the methyl groups at C-4 appeared in the range δ_C 20.3-17.6 ppm. The carbon atom of CF_3 group of **5** appeared as a doublet at δ_C 117.9 ppm ($J_{C,F}$ = 317.0 Hz).



4 **5** (75 %)

Scheme 1. *Reagents and conditions*: (i) Et_3N, CH_2Cl_2, 20 °C, then Tf_2O, -78 °C to 20 °C, 6 h.

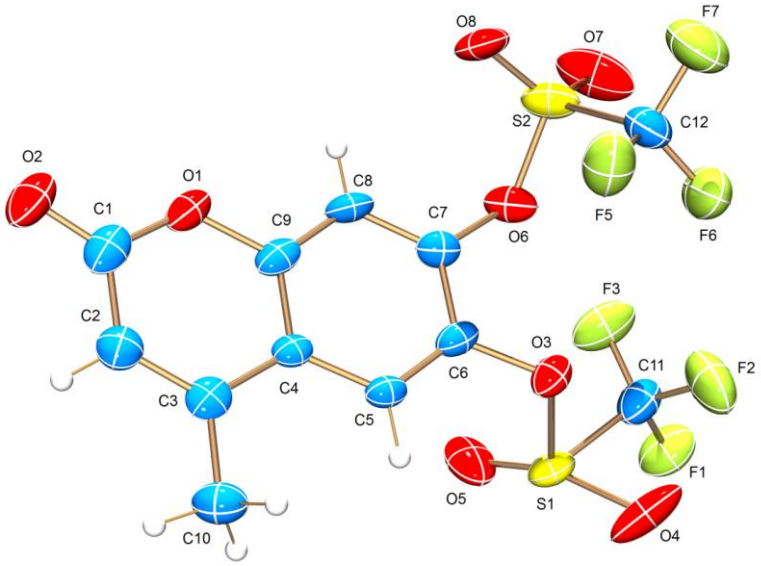


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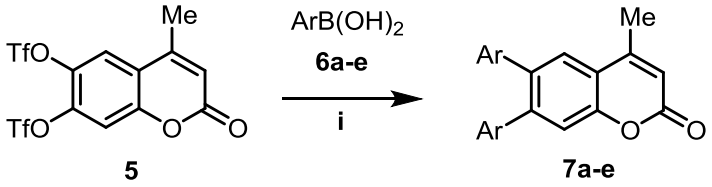
Figure 2. Molecular structure of **5** in the crystal. Displacement ellipsoids are drawn at the 30% probability level.



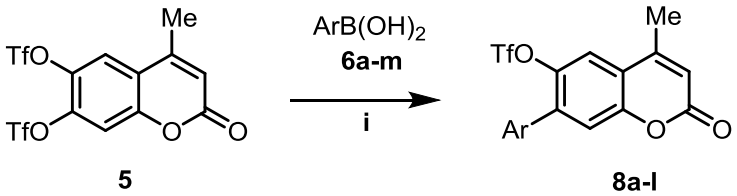
Scheme 2. Synthesis of **7a-e**. *Reagents and conditions*: (i) K_3PO_4, $Pd(PPh_3)_4$, 1,4-dioxane, 120 °C, 6 h.

Table 1. Synthesis of **7a-e**

6,7	**Ar**	**7** (%)[a]
a	3,5-$(Me)_2C_6H_3$	75
b	4-$MeOC_6H_4$	83
c	4-ClC_6H_4	83
d	C_6H_5	70
e	4-$EtOC_6H_4$	88

[a] Yields of isolated products

Treatment of **5** with arylboronic acids **6** (1.2 equiv.) *via* Suzuki-Miyaura reaction furnished 4-methyl-7-aryl-6-trifluorosulfonyloxy-coumarins **8a-l** in 70-90% yield with high site-selectivity (Scheme 3, Table 2). During the optimization, it proved to be important to use 1.2 equiv. of the arylboronic acid and to carry out the reaction at 70 °C instead of 120 °C to avoid double coupling. Both electron-poor and electron-rich arylboronic acids were successfully used.



Scheme 3. Synthesis of **8a-l**. *Reagents and conditions*: (i) K_3PO_4, $Pd(PPh_3)_4$, 1,4-dioxane, 70 °C, 6 h.

Table 2. Synthesis of **8a-m**

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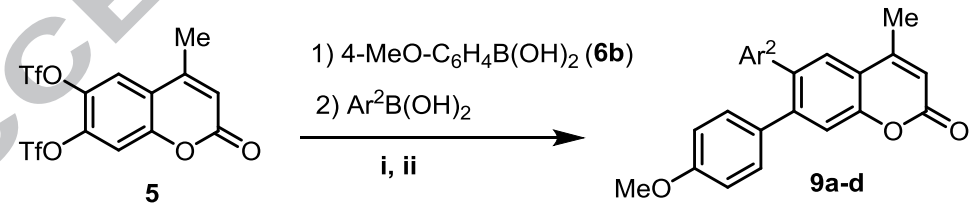
6,8	Ar	8 (%)[a]
a	3,5-$(Me)_2C_6H_3$	75
b	4-$MeOC_6H_4$	80
c	4-ClC_6H_4	85
d	C_6H_5	72
e	4-$EtOC_6H_4$	90
f	4-FC_6H_4	78
g	4-$(F_3C)C_6H_4$	83
h	4-MeC_6H_4	75
i	3-MeC_6H_4	80
j	3-$MeOC_6H_4$	70
k	2,3,4-$(MeO)_3C6H_2$	90
l	4-*t*BuC_6H_4	77

[a] Yields of isolated products

The one-pot Suzuki-Miyaura reaction of bis-triflate **5** with two different arylboronic acids **6** (sequential addition of 1.2 equiv. of each boronic acid) was next studied. Firstly, **5** was treated with 4-methoxphenylboronic acid (**6b**) (1.2 equiv.), followed by further treatment with arylboronic acids **6c,g,j,a** (1.2 equiv.) afforded the 4-methyl-6,7-diarylcoumarins **9a-d** in 73-81% yields, respectively. The reactions were carried out at 70 °C for the first step (to avoid double coupling) and at 120 °C in the second step (Scheme 4, Table 3).



Scheme 4. Synthesis of **9a-d**. *Reagents* and c*onditions*: (i) **6b** (1.2 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (3 mol-%), dioxane, 70 °C 6 h; (ii) $Ar^2B(OH)_2$ (1.2 equiv.), K_3PO_4 (1.5 equiv.), $Pd(PPh_3)_4$ (3 mol-%), 1,4-dioxane, 120 °C, 6 h.

Table 3. Synthesis of **9a-d**

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6	9	Ar^2	9 (%)[a]
b,c	**a**	4-ClC_6H_4	73
b,g	**b**	4-FC_6H_4	78
b,j	**c**	3-MeC_6H_4	75
b,a	**d**	3,5-$(Me)_2C_6H_3$	81

[a] Yields of isolated products

Compounds **8a-l** were identified from the ^{1}H NMR and ^{13}C NMR spectra, which showed almost similar resonances of benzopyran ring atoms as those of **7a-e**. H-3, and methyl group at C-4 appeared as two doublets with long range couplings in the regions δ_H 2.42-2.31 and 6.33-6.24 ppm, respectively ($J_{CH3,H3}$ ~ 1.3 Hz). H-5 and H-8 protons appeared as broad singlets in the regions δ_H 7.36-7.52 and 7.52-7.45 ppm, respectively. The aromatic protons resonated as multiplets or doublets between δ_H 7.47 and 6.80 ppm, while the other alkyl protons were fully analyzed.

In the ^{13}C-NMR spectra of **8a-l**, the resonances at δ_H 163.9-158.4 ppm were attributed to the carbonyl group (C-2). The carbon atoms C-3 and C-4 of the benzopyran ring resonated in the regions δ_H 115.6-113.8 and 158.6-150.9 ppm, respectively, while C-4a and C-5 appeared in the regions δ 119.5-115.5 and 117.5-115.1 ppm, respectively. C-6 - C-8a, aromatic and carbons of the other substituents carbon atoms were fully assigned (*cf.* Experimental section). Compound **8b** was selected for further NMR studies. In the gradient-selected HMBC spectrum [37] of **8b**, the olefinic proton (H-3) at δ_H 6.50 ppm showed two $^2J_{C,H}$ couplings: one to the carbonyl carbon atom of the the coumarin ring (C-2) at δ_C 160.9 ppm and the other coupling was with C-4 at δ_C 151.3 ppm. A $^3J_{C,H}$ between coupling between H-8 of coumarin ring at δ_H 6.60 ppm and aromatic carbon atom (C-1) at δ_C 136.8 ppm was assigned. Furthermore, in the NOESY spectrum,[38] a correlation between the protons of methyl group at C-4 and H-3 as well as between H-8 of coumarin ring and the aromatic protons H-2' and H-6' (Figure 3).

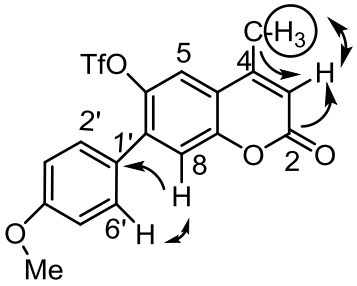

Figure 3. $J_{C,H}$ correlations in the HMBC (single head arrows), and NOESY (double head arrows) correlations of **8b**.

The ^{1}H NMR and ^{13}C NMR spectra of **9a-d** were in agreement with the suggested structures. The resonances of protons H-5 and H-8 appeared in the regions at δ_H 7.48-7.46 and 7.28-7.26 ppm, respectively, which differ from those of analogues **8a,c,f,i**, due to the substitution of the triflate

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group at C-6 by the aryl moieties. In the ^{13}C NMR spectra, carbon atoms C-5 and C-6 appeared in the regions δ_C 130.5-129.7 and 135.4-131.0 ppm, respectively, whereas carbon atoms C-8 were resonated in the region δ_C 117.8-117.1 ppm. Additional support of the proposed structures comes from mass spectral data; mass spectra of the prepared compounds showed the correct molecular ions as suggested by their molecular formulas. The structure of **8b** was independently confirmed by X-ray crystal structure analysis (Figure 4).

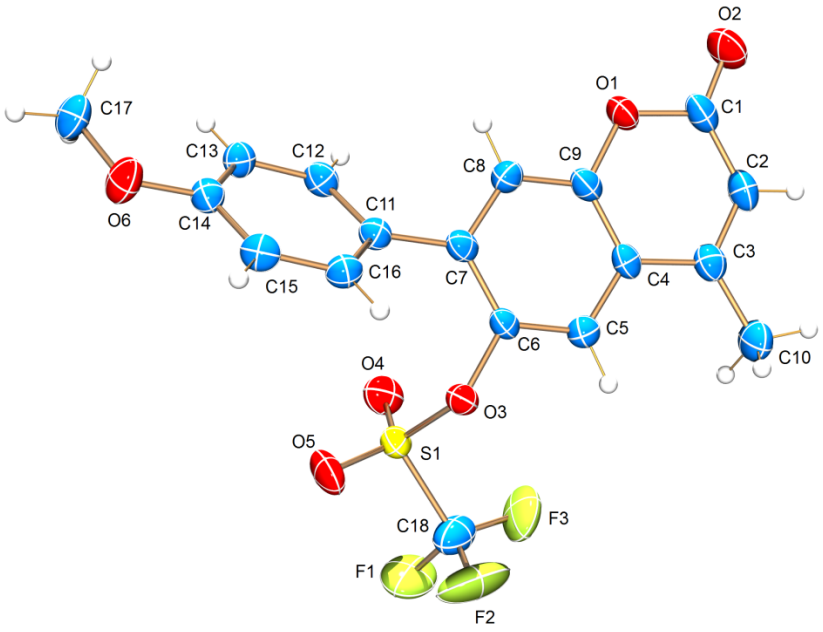
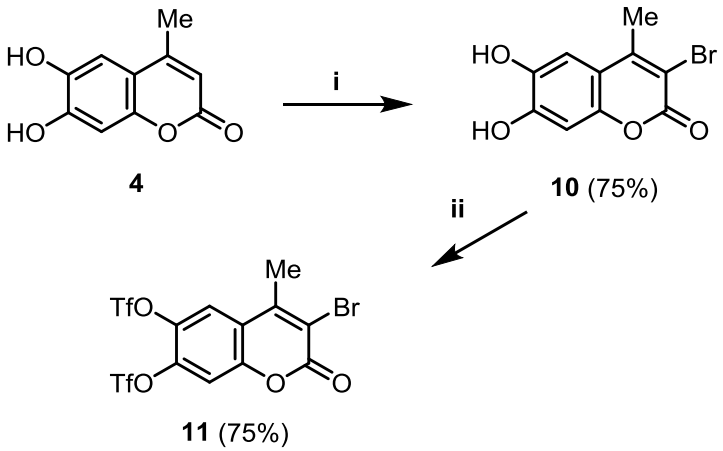


Figure 4. Molecular structure of **8b** in the crystal. Displacement ellipsoids are drawn at the 30% probability level.

Next, reaction of **4** with bromine afforded the brominated product **10** in 75% yield. The structure of **10** was independently confirmed by 2D NMR (Figure 5). Compound **10** was converted into bis-triflate **11**. The structure of **11** was independently confirmed by X-ray crystal structure analysis (Figure 6).



4 **10** (75%)

11 (75%)

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Scheme 5. Synthesis of **2.** *Reagents and conditions*: (i) **4** (1.0 equiv), Br_2 (2.0 equiv), AcOH, 30 °C, 2 h; (ii) **10** (1.0 equiv), Et_3N (4.0 equiv), CH_2Cl_2, 20 °C; then Tf_2O (2.4 equiv), -78 °C to 20 °C, 6 h.

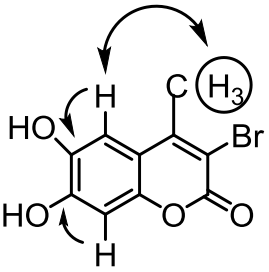

Figure 5. 2D NMR studies of **10**

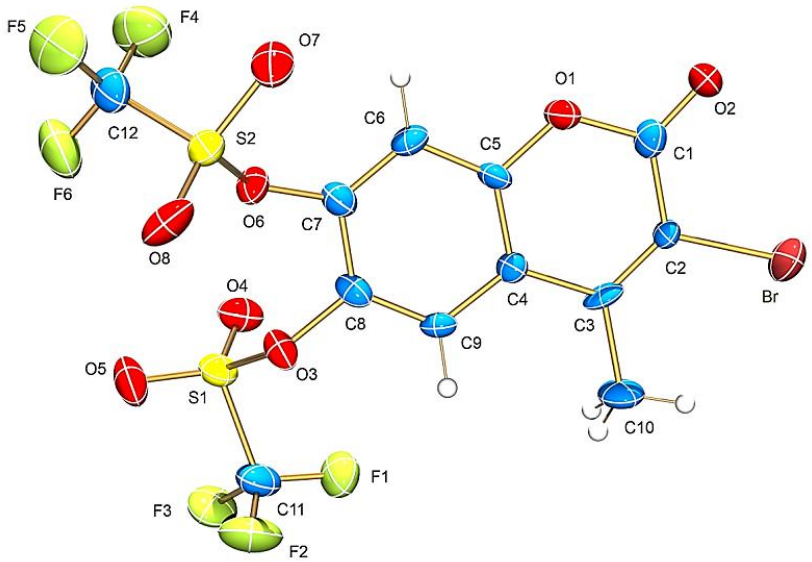

Figure 6. Molecular structure of **11** in the crystal. Displacement ellipsoids are drawn at the 50 % probability level.

Suzuki-Miyaura cross-coupling reaction of **11** with various arylboronic acids (3.1 equiv.) afforded the 4-methyl-3,6,7-tris(aryl)coumarines **12a-c and 12e-p** (Scheme 6, Table 4). Both electron-rich and electron-poor arylboronic acid were successfully employed. The yields of the products derived from arylboronic acids containing electron-withdrawing substituents, which are less nucleophilic, were lower than the yields of products derived from arylboronic acid containing electron-donating substituents. Unfortunately, all attempts to develop regioselective Suzuki-Miyaura reactions failed. This result is surprising, as substrate **11** is structurally very similar to substrate **5**. Substrate **11** only contains an additional bromine atom at position 3. The failure of the regioselective coupling can be explained by the fact that, in Suzuki-Miayaura reactions the bromine

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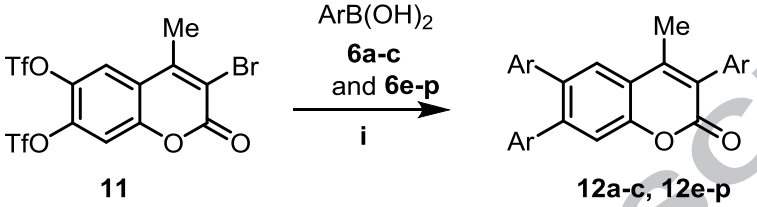
atom is a better leaving group than the triflate. Thus, there is a competition between positions 3 and 7 which results in the formation of mixtures. Position 3 possesses a better leaving group, but is sterically more hindered than position 7. Both positions 3 and 7 are more reactive than position 6. However, due to the formation of complex mixtures, it was also not possible to selectively address positions 3 and 7 by addition of two equivalents of a boronic acid.



Scheme 6. Synthesis of **12a-c** and **12e-p**. *Reagents and conditions:* (i) **6a-c, 6e-p** (3.1 equiv.), $Pd(PPh_3)_4$ (14 mg, 9 mol-%), K_2CO_3 (aq. solution, 2M), 1,4-dioxane, 120 °C, 10 h.

Table 4. Synthesis of **12a-c** and **12e-p**

6,12	Ar	**12** (%)[a]
a	3,5-$(Me)_2C_6H_3$	70
b	4-$MeOC_6H_4$	80
c	4-ClC_6H_4	60
e	4-$EtOC_6H_4$	84
f	4-FC_6H_4	70
g	4-$(F_3C)C_6H_4$	63
h	4-MeC_6H_4	75
i	3-MeC_6H_4	70
j	3-$MeOC_6H_4$	80
k	2,3,4-$(MeO)_3C6H_2$	80
l	4-*t*BuC_6H_4	62
m	3,4-$(Me)_2C_6H_3$	60
n	4-*i*PrC_6H_4	70
o	4-*i*$ProC_6H_4$	77
p	4-EtC_6H_4	75

[a] Yields of isolated products

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The conditions were optimized for synthesis of **12a** using various bases, such as K_2CO_3, KF, K_3PO_4 and NEt_3, different solvents, like toluene, DMF, dioxane and THF, and Pd sources, such as $Pb(OAc)_2$ and $Pd(PPh_3)_2Cl_2$ at various temperatures (65-130 °C) (Table 5).

Table 5. Optimization of synthesis of **12a**

Entry	Base	Solvent	T (^{o}C)	Catalyts	T (h)	Yield (%)[a]
1	K_3PO_4	Toluene	100	$Pd(OAc)_2$	8	25
2	K_2CO_3	DMF	130	$Pd(PPh_3)_4$	9	38
3	KF	Dioxane	80	$Pd(OAc)_2$	10	47
4	NEt_3	THF	65	$Pd(PPh_3)_2Cl_2$	7	34
5	K_2CO_3	Dioxane	120	$Pd(PPh_3)_4$	10	84
6	K_2CO_3	Toluene	90	$Pd(OAc)_2$	9	25

[a] Yields of isolated products.

The structure of **12f** was independently confirmed by 2D NMR (Figure 7), meanwhile the structure of **12g** was independently confirmed by X-ray crystal structure analysis (Figure 8).

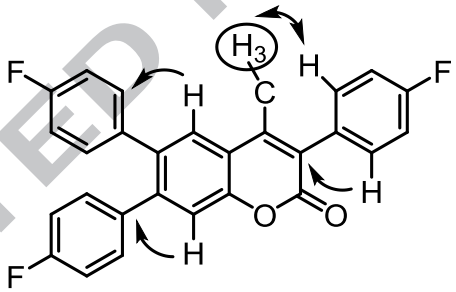

Figure 7. $J_{C,H}$ correlations in the HMBC (single head arrow), and NOESY (double head arrow) correlations of **12f**.

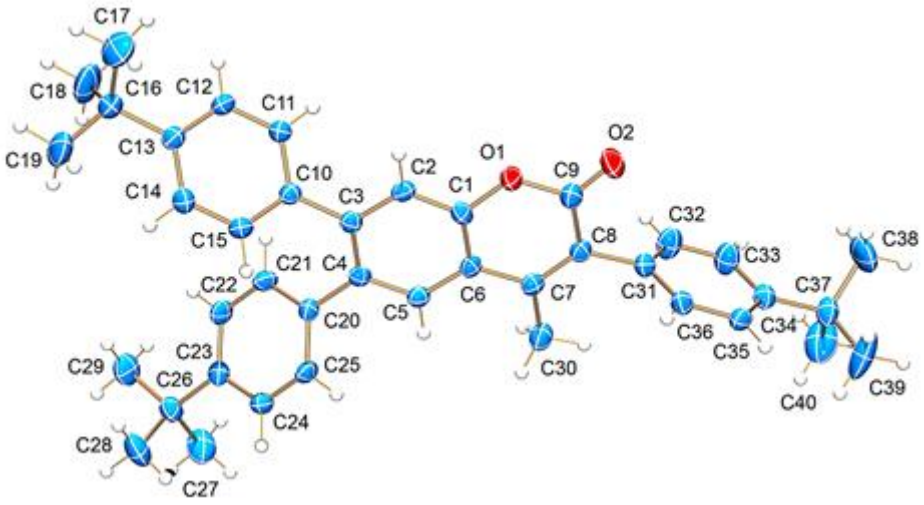

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Figure 8. Molecular structure of **12g** in the crystal. Displacement ellipsoids are drawn at the 50 % probability level.

2.2. *In vitro* anti-HIV activity

Compounds **5**, **7a-e**, **8a-l** and **9a-d** were tested for their *in vitro* anti-HIV-1 (strain III_B) and HIV-2 (strain ROD) activity in human (MT-4) cells based on an MTT assay (Table 6).[39,40] Derivatives **12a-c** and **12e-p** showed a relatively low solubility and where, therefore, not tested. The results are summarized in Table 6, in which the data for nevirapine (BOE/BIRG587)[41] and azidothymidine (DDN/AZT)[42] are included for comparison purposes. Compound-induced cytotoxicity was also measured in MT-4 cells parallel with the antiviral activity. Compounds **7a** and **8i** were found to be the only compounds from the series inhibiting HIV-1 replication in a cell culture, which showed an IC_{50} of 4.57 μg mL^{-1} and 13.20 μg mL^{-1} with CC_{50} of 14.40 μg mL^{-1} and 61.34 μg mL^{-1}, respectively, resulting in a selectivity index of 3 and 5. On the other hand, **8k**, **9a**, and **9d** showed some activity against HIV-1 (III_B strain) with IC_{50} > 2.13, > 2.06 and > 2.08 μg mL^{-1}, respectively, but no selectivity was witnessed (SI < 1). However, implantation of methyl groups in 3 and 5 positions of both phenyl groups at C-6 and C-7 of the coumarin ring (compound **7a**) or methyl group in 3 position of phenyl residue at C-7 together with the triflate at C-6 of the coumarin ring (compound **8i**) considerably increased the anti-HIV activity, in comparison to the effectiveness of other functional groups. In conclusion, the anti-HIV activity and the selectivity of these compounds are too limited to perform extensive mode-of-action studies, and **7a** and **8i** might be considered as a new lead in the development of antiviral agents as non-nucleoside reverse transcriptase inhibitors.

Table 6. *In vitro* anti-HIV-1[a] and HIV-2[b] activity and cytotoxicity of some new coumarins

Entry	HIV-1 (III_B) IC_{50} (μg mL^{-1})[c]	HIV-2 (ROD) IC_{50} (μg mL^{-1})[c]	CC_{50} (μg mL^{-1})[d]	SI[e] (III_B)	SI[e] (ROD)
5	>43.50	>43.50	43.50	<1	<1
7a	4.57	>14.40	14.40	3	<1
7b	>11.00	>11.00	11.00	<1	<1
7c	>15.98	>15.98	15.98	<1	<1
7d	>13.78	>13.78	13.78	<1	<1
7e	>37.31	>37.31	37.31	<1	<1
8a	>33.10	>33.10	33.10	<1	<1
8b	>10.60	>10.60	≥10.60	<orX1	<orX1

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8c	>30.65	>35.65	35.65	<1	<1
8d	>12.55	>12.55	12.55	<1	<1
8e	>27.20	>27.20	≥27.20	<orX11	<orX1
8f	>10.63	>10.63	10.63	<1	<1
8g	>80.33	>80.33	80.33	<1	<1
8h	>11.00	>11.00	11.00	<1	<1
8i	13.20	>61.34	61.34	5	<1
8j	>18.86	>18.86	18.86	<1	<1
8k	>2.13	>2.13	2.13	<1	<1
8l	>10.28	>10.28	10.28	<1	<1
9a	>2.06	>2.06	2.06	<1	<1
9b	>10.92	>10.92	10.92	<1	<1
9c	>7.40	>7.40	7.40	<1	<1
9d	>2.08	>2.08	2.08	<1	<1
Nevirapine	0.050	>4.00	>4.00	>80	<1
AZT	0.0022	0.00094	>25	>11363	>26596

[a] Anti-HIV-1 activity measured with strain III_B; [b] anti-HIV-2 activity measured with strain ROD; [c] compound concentration required to achieve 50% protection of MT-4 cells from the HIV-1 and HIV-2-induced cytopathic effect; [d] compound concentration that reduces the viability of mock-infected MT-4 cells by 50 %; [e] SI: selectivity index (CC_{50}/IC_{50}).

3. Conclusion

In conclusion, we have reported a new synthesis of arylated coumarins by site-selective Suzuki-Miyaura cross-coupling reactions. The synthesized compounds were evaluated for their *in vitro* anti-HIV inihibitory activity. Two derivatives show considerable activities and can be regarded as lead structures for further investigations. However, the selectivity and activity are so far not sufficient to carry out mode-of-action studies which will be done in future studies along with additional screening experiments.

4. Experimental

Melting points are uncorrected and were determined on a Micro heating table HMK 67/1825 Kuestner (Buchi Apparatus), and a Leitz Labolux 12 Pol with heating table Mettler FP 90. FT-IR spectra were recorded on a Nicolet 205 FT-IR and Nicolet Prot´ege 460 FT-IR instruments using the KBr technique. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.5 MHz) spectra were measured on

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Bruker AC 250, Bruker ARX 300 and Bruker ARX 500 instruments in DMSO-d_6 as a solvent. Mass spectra (MS) were run on AMD MS40, Varian MATCH 7, MAT 731 (EI, 70 eV), Intecta AMD 402, (EI, 70 eV and CI), and Finnigan MAT 95 (CI, 200 eV) spectrometers. High-resolution mass spectrometry (HRMS) was performed on Varian MAT 311 and Intecta AMD 402 instruments. The X-ray crystal structure analyses were deposited at the CCDC.[46]

4.1. Chemistry

4.1.1. 6,7-Bis(trifluoromethanesulphonyl)-4-methyl-2*H*-chromen-2-one (**5**)

To a solution of 4-methyl-6,7-dihydroxycoumarin (**4**) (0.50 g, 2.60 mmol) in CH_2Cl_2 (30 mL) was added Et_3N (0.36 mL, 10.4 mmol) at room temperature under an argon atmosphere. After 10 min, Tf_2O (1.0 mL, 6.20 mmol) was added at -78 °C. The mixture was allowed to warm to 20 °C and stirred for 6 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptane / EtOAc = 4 :1) without aqueous work up to give **5** as a white solid (0.90 g, 75%); mp: 125-127 °C. IR (KBr, cm^{-1}): *v* 3124, 3053, 2964, 2926 (w), 1740 (s), 1673, 1625, 1613, 1570 (w), 1498 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.41 (d, $J_{CH3,H3}$ = 1.5 Hz, CH_3), 6.37 (d, 1H, H-3), 7.41 (br s., 1H, H-5), 7.59 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 18.6 (CH_3), 110.9 (C-8), 112.7 (C-3 + C-4a), 113.1 (C-5), 117.9 (d, $J_{C,F}$ = 317.0 Hz, CF_3), 136.4 (C-6), 141.7 (C-7), 150.5 (C-8a), 152.6 (C-4), 158.2 (CO). ^{19}F NMR (282.4, MHz) δ: - 72.8, - 72.7. GC-MS (EI, 70 eV): *m/z* (%) = 456 ($[M]^+$, 100), 324 (10), 323 (84), 232 (10), 203 (33), 162 (13), 134 (26), 69 (55). HRMS (EI, 70 eV) calcd for $C_{12}H_6F_6O_8S_2$ ($[M]^+$): 455.94028; found: 455.94130.

4.1.2. General procedure for the preparation of 6,7-bis(aryl)-4-methyl-2*H*-chromen-2-one (**7a-e**)

To a dioxane suspension (3 mL) of bis(triflate) analogue **5** (70 mg, 0.15 mmol), $Pd(PPh_3)_4$ (11 mg, 6 mol -%, 0.0092 mmol), and arylboronic acids **6** (0.34 mmol) was added K_3PO_4 (98 mg, 0.46 mmol). The mixture was heated at 120 ^{o}C under Argon atmosphere for 6 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (3x25 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (silica gel, EtOAc / heptane).

4.1.2.1. 6,7-Bis(3,5-dimethylphenyl)-4-methyl-2*H*-chromen-2-one (**7a**)

From 3,5-dimethylphenylboronic acid (**6a**) (51 mg). Yield: 42 mg (75%) as a white solid, mp: 121-122 °C. IR (KBr, cm^{-1}): *v* 3015, 3082, 3066, 2868, 2732, 2645 (w), 1722 (s), 1618, 1607 (m), 1573,

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1537, 1516, 1485 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.13 (s, 6H, 2xCH_3), 2.14 (s, 6H, 2xCH_3), 2.39 (d, 3H, $J_{CH3,H3}$ = 1.3 Hz, CH_3), 6.24 (d, 1H, H-3), 6.67-6.80 (m, 6H, ArH), 7.30 (br s., 1H, H-8), 7.49 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (2xCH_3), 20.1 (2xCH_3), 26.1 (CH_3), 113.9 (C-3), 117.7 (C-8), 120.1 (C-4a), 125.1, 126.4, 126.6, 127.4, 127.9 (Carom + C-5 + C-6), 136.3 (C-7), 138.5, 139.1 (C_{arom}), 151.2 (C-8a), 154.4 (C-4), 160.9 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 368 ([M]$^+$, 100), 353 (12), 338 (10). HRMS (EI, 70 eV) calcd for $C_{26}H_{24}O_2$:368.17708 [M]$^+$; found: 368.17685.

4.1.2.2. 6,7-Bis(4-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (**7b**)

From 4-methoxyphenylboronic acid (**6b**) (52 mg). Yield: 47 mg (83%) as a white solid, mp: 103-105 °C. IR (KBr, cm^{-1}): *v* 3115, 3092, 3076, 2968, 2932, 2845 (w), 1732 (s), 1628, 1607 (m), 1583, 1547, 1526, 1495 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.38 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 3.72 (s, 6H, 2xOCH_3), 6.23 (d, 1H, H-3), 6.69-6.74 (m, 4H, ArH), 6.97-7.01 (m, 4H, ArH), 7.27 (br s., 1H, H-8), 7.47 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 18.6 (CH_3), 55.2 (2xOMe), 113.6 (C-3), 114.8 (C_{arom}), 118.2 (C-8), 118.6 (C-4a), 126.3, 130.7, 130.8, 132.1, 132.7 (C_{arom} + C-5 + C-6), 136.6 (C-7), 152.1 (C-8a), 152.5 (C-4), 158.6, 158.8 (2xC_{arom}-OMe), 160.9 (CO). GC-MS (EI, 70 e): *m/z* (%) = 372 ([M]$^+$, 100), 357 (12), 341 (11), 229 (10). HRMS (EI, 70 eV) calcd for $C_{24}H_{20}O_4$: 372.13561 [M]$^+$; found: 372.13535.

4.1.2.3. 6,7-Bis(4-chlorophenyl)-4-methyl-2*H*-chromen-2-one (**7c**)

From 4-chlorophenylboronic acid (**6c**) (53 mg). Yield: 49 mg (83%) as a white solid, mp: 221-222 °C. IR (KBr, cm^{-1}): *v* 3065, 2959, 2922, 2852 (w), 1727, 1715 (s), 1621, 1614 (m), 1594, 1573, 1568, 1543, 1510, 1505, 1479 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (d, 3H, $J_{CH3,H3}$= 1.3 Hz, CH_3), 6.27 (d,1H, H-3), 6.97-6.99 (m, 4H, ArH), 7.15-7.19 (m, 4H, ArH), 7.28 (br s., 1H, H-8), 7.48 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (CH_3), 114.5 (C-3), 117.5 (C-8), 118.3 (C-4a), 125.4, 127.4, 127.5, 129.8, 130.0, 132.4, 132.9, 134.7 (C_{arom} + C-5 + C-6), 136.7 (C-7), 137.2, 142.0 (C_{arom}), 150.8 (C-8a), 151.8 (C-4), 159.4 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 380 ([M]$^+$, [Cl] ^{35}, [Cl] ^{35}, 100), 352 (11), 252 (18), 253 (13). HRMS (EI, 70 eV) calcd for $C_{22}H_{14}Cl_2O_2$[Cl]^{35}, [Cl] ^{35}): 380.03654 ([M]$^+$; found: 380.03632.

4.1.2.4. 4-Methyl-6,7-diphenyl-2*H*-chromen-2-one (**7d**)

From phenylboronic acid (**6d**) (42 mg). Yield: 34 mg (70%) as a white solid, mp: 163-165 °C. IR (KBr, cm^{-1}): *v* 3110, 3087, 3071, 2963, 2927, 2840 (w), 1727 (s), 1623, 1602 (m), 1578, 1542, 1521, 1490 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (d, 3H, $J_{CH3,H3}$ = 1.1 Hz, CH_3), 6.25 (d,1H, H-3), 7.04-7.07 (m, 4H, ArH), 7.16-7.18 (m, 6H, ArH), 7.33 (br s., 1H, H-8), 7.53 (br s., 1H, H-5). ^{13}C

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NMR (75.46 MHz, $CDCl_3$) δ:18.6 (CH_3), 115.1 (C-3), 118.5 (C-4a + C-8), 126.4, 126.9, 127.4, 128.1, 129.6, 129.8 (C_{arom} + C-5 + C-6), 137.1 (C-7), 139.6, 144.4 (C_{arom}), 152.1 (C-8a), 153.6 (C-4), 160.8 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 312 ($[M]^+$, 100), 311 (12), 284 (11), 283 (15), 252 (10), 239 (17). HRMS (EI, 70 eV) calcd for $C_{22}H_{16}O_2$: 312.11448 $[M]^+$; found: 312.11468.

4.1.2.5. 6,7-Bis(4-ethoxyphenyl)-4-methyl-2*H*-chromen-2-one (**7e**)

From 4-ethoxyphenylboronic acid (**6e**) (57 mg). Yield: 54 mg (88%) as a white solid, mp: 188-190 °C. IR (KBr, cm^{-1}): *v* 3118, 3093, 3079, 2971, 2935, 2848 (w), 1735 (s), 1631, 1609 (m), 1585, 1549, 1528, 1497 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.33 (t, 6H, J = 6.5 Hz, 6H, 2xCH_2CH_3), 2.38 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 3.94 (q, 4H, J = 6.9 Hz, 2xCH_2CH_3), 6.22 (d,1H, H-3), 6.68-6.72 (m, 4H, ArH), 6.95-6.90 (m, 4H, ArH), 7.27 (br s., 1H, H-8), 7.46 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ:13.8, 17.6 (2xCH_2CH_3), 20.3 (CH_3), 62.3 (2xCH_2CH_3), 113.2 (C-3), 113.8, 114.4 (C_{arom}), 117.2 (C-8), 117.6 (C-4a), 125.2, 129.7, 129.8, 130.9, 131.6 (C_{arom} + C-5+ C-6) , 135.7 (C-7), 151.2 (C-8a), 151.5 (C-4), 157.0, 157.3 (2xC^4_{arom}-OEt), 160.9 (CO). GC-MS (EI,70 eV): *m/z* (%) = 400 ($[M]^+$, 100), 344 (15). HRMS (EI, 70 eV) calcd for $C_{26}H_{24}O_4$: 400.16691 $[M]^+$; found: 400.16654.

4.1.3. General procedure for the preparation of 7-aryl-4-methyl-6-O-trifluoromethane sulphonyl-2*H*-chromen-2-one (**8a-l**)

Method was analogous to the procedure for preparation of **7a-e**, using instead arylboronic acid **6a-l** (1.2 equiv., 0.18 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol -%, 0.005 mmol) and K_3PO_4 (49 mg, 0.23 mmol).

4.1.3.1. 7-(3,4-Dimethylphenyl)-4-methyl-6-O-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8a**)

From 3,5-dimethylphenylboronic acid (**6a**) (27 mg). Yield: 47 mg (75%) as a white solid, mp: 165-167 °C. IR (KBr, cm^{-1}): *v* 3057, 2950, 2910, 2838 (w), 1721 (s), 1611, 1606 (m), 1538 (w), 1509, 1491 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.45 (s, 6H, 2xCH_3), 2.31 (d, 3H, $J_{CH3,H3}$ = 1.4 Hz, CH_3), 6.31 (d, 1H, H-3), 7.17 (m., 3H, ArH), 7.33 (d, 1H, H-5), 7.48 (br s., 1H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$) δ: 17.6 (2xCH_3), 20.1 (CH_3), 113.9 (C-3), 115.2 (C-5), 118.7 (C-4a), 125.4 (q, $J_{C,F}$ = 320.4 Hz, CF_3), 126.4 (C-8), 127.9 (C-7), 129.8, 132.8, 136.3, 137.3, 138.4 (C_{arom}), 141.5 (C-8a), 149.8 (C-6), 151.3 (C-4), 160.1 (CO). ^{19}F NMR (282.4, MHz) δ: - 73.8. GC-MS (EI, 70 eV): *m/z* (%) = 412 ($[M]^+$, 100), 280 (20), 279 (30), 264 (12), 235 (11). HRMS (EI, 70 eV) calcd for $C_{19}H_{15}F_3O_5S$: 412.05868 $[M]^+$; found: 412.05840.

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4.1.3.2. 7-(4-Methoxyphenyl)-4-methyl-6-*O*-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8b**)

From 4-methoxyphenylboronic acid (**6b**) (27 mg). Yield: 50 mg (80%) as a white solid, mp: 134-136 °C. IR (KBr, cm^{-1}): *v* 3112, 3089, 3074, 2965, 2929, 2841 (w), 1729 (s), 1621, 1605 (m), 1576, 1543, 1520, 1491 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.39 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 3.80 (s, 3H, OMe), 6.30 (d, 1H, H-3), 6.93 (d, 2H, $J_{3,5}$ = 8.9 Hz, $ArH^{3,5}$), 7.33-7.37 (m, 3H, ArH + H-5), 7.48 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 18.5 (CH_3), 55.3 (OMe), 114.3 (C-3), 116.1 (C-5), 118.4 (C_{arom}), 119.1 (q, $J_{C,F}$ = 320.1 Hz, CF_3), 119.5 (C-4a), 120.4 (C-8), 126.3 (C-7), 130.6, 138.8 (C_{arom}), 142.6 (C-8a), 150.9 (C-4), 152.4 (C-6), 159.7 (C_{arom}-OMe), 160.9 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ: - 73.6. GC-MS (EI, 70 eV): *m/z* (%) = 414 ($[M]^+$, 100), 282 (20), 281 (30). HRMS (EI, 70 eV) calcd for $C_{18}H_{13}F_3O_6S$: 414.03794 $[M]^+$; found: 414.03813.

4.1.3.3. 7-(4-Chlorophenyl)-4-methyl-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8c**)

From 4-chlorophenylboronic acid (**6c**) (28 mg). Yield: 55 mg (85%) as a white solid, mp: 124-125 °C. IR (KBr, cm^{-1}): *v* 3080, 3065, 2921, 2850 (w), 1738, 1732, 1615 (s), 1592, 1574, 1538 (w), 1505 (m), 1477 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (d, 3H, $J_{CH3,H3}$ = 1.1 Hz, CH_3), 6.33 (d, 1H, H-3), 6.96-7.42 (m, 6H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ:17.6 (CH_3), 115.6 (C-3 + C-5), 117.5 (q, $J_{C,F}$ = 320.3 Hz, CF_3), 119.3 (C-4a), 128.1 (C-8), 129.4 (C-7), 129.6, 131.4, 134.6, 136.7, 141.3 (C_{arom}), 144.7 (C-8a), 150.0 (C-6), 151.3 (C-4), 158.4 (CO). ^{19}F NMR (282.4 MHz) δ: - 73.5. GC-MS (EI, 70 eV): *m/z* (%) = 418 ($[M]^+$, [^{35}Cl], 100), 287 (34), 285 (20), 251 (10), 222 (41), 165 (25). HRMS (EI, 70 eV) calcd for $C_{17}H_{10}O_5{}^{35}ClF_3S$: 417.98841 $[M]^+$; found: 417.98743.

4.1.3.4. 4-Methyl-7-phenyl-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8d**)

From phenylboronic acid (**6d**) (22 mg). Yield: 42 mg (72%) as a white solid, mp: 95-96 °C. IR (KBr, cm^{-1}): *v* 3090, 2981, 2941, 2869 (w), 2981 (s), 2925, 2875 (m), 1568 (w), 1529, 1496 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.40 (s, 3H, CH_3), 6.26 (s, 1H, H-3), 7.07-7.18 (m, 5H, ArH + H-5), 7.53 (br s., 1H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$) δ: 17.6 (CH_3), 114.2 (C-3), 117.5 (C-5 + C-4a), 117.7 (q, $J_{C,F}$ = 320.2 Hz, CF_3), 125.4 (C-8), 126.4 (C-7), 127.7 128.2, 128.8, 136.1, 138.6, 139.2 (C_{arom}), 143.4 (C-8a), 151.1 (C-6), 151.7 (C-4), 159.8 (CO). ^{19}F NMR (282.4, MHz) δ: - 73.7. GC-MS (EI, 70 eV): *m/z* (%) = 384 ($[M]^+$, 100), 252 (18), 251 (30), 195 (19), 152 (13). HRMS (EI, 70 eV) calcd for $C_{17}H_{11}F_3O_5S$ $[M]^+$: 384.02738; found: 384.02760.

4.1.3.5. 7-(4-Ethoxyphenyl)-4-methyl-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8e**)

From 4-ethoxyphenylboronic acid (**6e**) (30 mg). Yield: 59 mg (90%) as a white solid, mp: 122-124 °C. IR (KBr, cm^{-1}): *v* 3119, 3081, 2988, 2923, 2852 (w), 1728 (s), 1660 (w), 1607 (m), 1576, 1542,

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1522, 1496 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.48 (t, 3H, J = 6.9 Hz, $CH_2\mathit{CH_3}$), 2.39 (s, 3H, $J_{CH3,H3}$ = 1.6 Hz, CH_3), 4.03 (q, 2H, J = 6.9 Hz, $\mathit{CH_2}CH_3$), 6.29 (d, 1H, J = 1.6 Hz , H-3), 6.92 (d, 2H, J = 8.8 Hz, ArH^{3,5}), 7.29-7.39 (m, 3H, ArH + H-5), 7.48 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 18.4 ($CH_2\mathit{CH_3}$), 18.6 (CH_3), 63.5 ($\mathit{CH_2}CH_3$), 114.7 (C-3 + C_{arom}), 116.0 (C-5), 117.3 (C-4a), 118.2 (q, $J_{C,F}$ = 320.0 Hz, CF_3), 119.5 (C-8), 127.3 (C-7), 130.5, 138.8 (C_{arom}), 142.6 (C-8a), 151.9 (C-4), 152.5 (C-6), 158.2 ($\mathit{C_{arom}}$-OEt), 159.8 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -73.7. GC-MS (EI, 70 eV): *m/z* (%) = 428 ([M]$^+$, 100), 296 (19), 295 (30), 267 (69). HRMS (EI, 70 eV) calcd for $C_{19}H_{15}F_3O_6S$: 428.05359 [M]$^+$; found: 428.05397.

4.1.3.6. 7-(4-Fluorophenyl)-4-methyl-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8f**)

From 4-fluorophenylboronic acid (**6f**) (25 mg). Yield: 48 mg (78%) as a white solid, mp: 111-112 °C. IR (KBr, cm^{-1}): *v* 3022, 2961, 2918, 2851 (w), 1731, 1715 (s), 1651 (w), 1621, 1610 (m), 1573, 1568, 1543, 1519, 1514, 1485 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.38 (d, 3H, $J_{CH3,H3}$ = 1.3 Hz, CH_3), 6.23 (d, 1H, H-3), 6.94-6.98 (m, 4H, ArH), 7.29 (br s., 1H, H-5), 7.49 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (CH_3), 114.1 (C-3), 117.4 (C-5), 117.8 (C-4a + C-8), 118.8 (q, $J_{C,F}$ = 320.1 Hz, CF_3), 127.8, 128.6 (2xd, J = 21.6, 8.2 Hz, C_{arom}-F + C-7), 136.0 (d, J = 3.3 Hz, C^1_{arom}-F), 143.4 (C-8a), 146.8 (d, $J_{C,F}$ = 248.9 Hz, C_{arom}-F), 151.7 (C-4 + C-6), 159.9 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ: - 112.4, -73.8. GC-MS (EI, 70 eV): *m/z* (%) = 402 ([M]$^+$, 100), 270 (17), 269 (30), 165 (12). HRMS (EI, 70 eV) calcd for $C_{17}H_{10}F_4O_5S$: 402.01796 [M]$^+$; found: 402.01766.

4.1.3.7. 4-Methyl-7-(4-(trifluoromethanephenyl)-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8g**)

From 4-trifluoromethanephenylboronic acid (**6g**) (34 mg). Yield: 58 mg (83%) as a white solid, mp: 101-102 °C. IR (KBr, cm^{-1}): *v* 3053, 2961, 2905, 2854 (w), 1723, 1614 (s), 1574, 1547, 1488 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.42 (d, 3H, $J_{CH3,H3}$ = 1.3 Hz, CH_3), 6.30 (d, 1H, H-3), 7.17 (d, 2H, $J_{2,6}$ = 8.1 Hz, ArH^{2,6}), 7.33 (br s., 1H, H-5), 7.46 (d, 2H, $J_{3,5}$ = 8.1 Hz, ArH^{3,5}), 7.54 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (CH_3), 114.9 (C-3), 117.8 (C-5), 118.8 (C-4a + C-8), 122.2 (q, $J_{C,F}$ = 320.4 Hz, SO_2CF_3), 124.3 (d, $J_{Carom,F}$ = 21.6 Hz, C^3_{arom}), 125.7 (d, $J_{Carom,F}$ = 8.2 Hz, C^3_{arom} + C-7), 135.6 (d, $J_{Carom,F}$ = 32.6 Hz, $\mathit{C^4arom}$-CF_3), 135.8, 136.4 (C_{arom}), 143.4 (C-8a), 146.8 (d, $J_{C,F}$ = 248.9 Hz, CF_3), 151.7 (C-6), 152.1 (C-4), 159.9 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -112.4, -62.6. GC-MS (EI, 70 eV): *m/z* (%) = 452 ([M]$^+$, 100), 270 (17), 269 (30), 165 (12). HRMS (EI, 70 eV) calcd for $C_{18}H_{10}F_6O_5S$: 452.01476 [M]$^+$; found: 452.12567.

4.1.3.8. 4-Methyl-7-(4-methylphenyl)-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8h**)

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From 4-methylphenylboronic acid (**6h**) (25 mg). Yield: (46 mg (75%) as a white solid, mp: 135-136 °C.IR (KBr, cm^{-1}): *v* 3067, 2960, 2920, 2848 (w), 1731 (s), 1621, 1606 (m), 1548 (w), 1519, 1491 (m). ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 2.25 (s, 3H, CH_3), 2.40 (d, 1H, $J_{CH3,H3}$ = 1.3 Hz, 3H, CH_3), 6.32 (d, 1H, H-3), 7.11 (d, 2H, $J_{3,5}$ = 8.2 Hz, $ArH^{3,5}$), 7.32 (br s., 1H, H-5), 7.47 (d, 2H. $J_{2,6}$ = 8.3 Hz, $ArH^{2,6)}$, 7.50 (br s., 1H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$) *δ*: 17.5, 17.6 (2xCH_3), 114.8 (C-3), 115.1 (C-5), 115.5 (C-4a), 117.2 (C-8), 118.5 (q, $J_{C,F}$ = 319.4 Hz, CF_3), 130.3 (C-7 + C_{arom}), 136.9 , 141.4 (C_{arom}), 149.7 (C-8a), 151.3 (C-4 + C-6), 162.9 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) *δ*: - 73.5. GC-MS (EI, 70 eV): *m/z* (%) = 398 ($[M]^+$, 100), 265 (16), 238 (17), 237 (85), 209 (34), 165 (32). HRMS (EI, 70 eV) calcd for $C_{18}H_{13}F_3O_5S$: 398.04303 $[M]^+$; found: 398.04309.

4.1.3.9. 4-Methyl-7-(3-methylphenyl)-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (8i)

From 3-methylphenylboronic acid (**6i**) (25 mg). Yield: 48 mg (80%) as a white solid, mp: 85-86 °C. IR (KBr, cm^{-1}): *v* 3070, 2961, 2921, 2849 (w), 2961 (s), 2905, 2855 (m), 1548 (w), 1519, 1491 (m). ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 2.20 (s, 3H, CH_3), 2.39 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 6.24 (d, 1H, H-3), 6.80 (d, 2H, *J* = 8.3 Hz, ArH), 7.01-7.03 (m, 2H, ArH), 7.31 (br s., 1H, H-5), 7.50 (br s., 1H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$) *δ*: 17.5, 17.6 (2xCH_3), 114.8 (C-3), 115.1 (C-5), 115.5 (C-4a), 118.5 (C-8), 118.7 (q, $J_{C,F}$ = 319.4 Hz, CF_3), 130.3 (C-7 + C_{arom}), 136.9, 141.4 (C_{arom}), 151.3 (C-8a), 151.5 (C-6), 152.6 (C-4), 163.9 (CO). ^{19}F NMR (282.4, MHz) *δ*: - 73.7. GC-MS (EI, 70 eV): *m/z* (%) = 398 ($[M]^+$, 100), 266 (18), 265 (30), 209 (11). HRMS (EI, 70 eV) calcd for $C_{18}H_{13}F_3O_5S$: 398.04303 $[M]^+$; found: 398.04297.

4.1.3.10. 7-(3-Methoxyphenyl)-4-methyl-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (8j)

From 3-methoxyphenylboronic acid (**6j**) (27 mg). Yield: 44 mg (70%) as a white solid, mp: 112-114 °C. IR (KBr, cm^{-1}): *v* 3112, 3089, 3074, 2965, 2929, 2841 (w), 1731 (s), 1621, 1600, 1582 (m), 1547, 1506, 1482, 1468 (w). ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 2.40 (d, 3H, $J_{CH3,H3}$ = 1.3 Hz, CH_3), 3.78 (s, 3H, OMe), 6.32 (d, 1H, H-3), 6.91-6.93 (m, 2H, ArH), 6.95 (d, 1H, *J* = 8.8 Hz, ArH), 7.30 (d, 1H, *J* = 8.8 Hz 1H, ArH), 7.36 (br s., 1H, H-5), 7.49 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) *δ*: 17.5 (CH_3), 54.3 (OMe), 113.8 (C-3), 115.1 (C-5), 115.4 (C-4a), 118.8 (C-8), 119.1 (q, $J_{C,F}$ = 320.1 Hz, CF_3), 128.8 (C-7 + C_{arom}), 134.2, 137.9, 141.5 (C_{arom}), 151.3 (C-8a), 158.6 (C-4 + C-6), 159.1 (C_{arom}-OMe), 160.9 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) *δ*: - 73.7. GC-MS (EI, 70 eV): *m/z* (%) = 414 ($[M]^+$, 100), 282 (18), 281 (40), 67 (18). HRMS (EI, 70 eV) calcd for $C_{18}H_{13}F_3O_6S$: 414.03794 $[M]^+$; found: 414.03799.

4.1.3.11. 4-Methyl-7-(2,3,4-trimethoxyphenyl)-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (8k)

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From 2,3,4-trimethoxyphenylboronic acid (**6k**) (38 mg). Yield: 65 mg (90%) as a white solid, mp: 155-157 °C. IR (KBr, cm^{-1}): *v* 3110, 3087, 3072, 2963, 2927, 2839 (w), 1727 (s), 1619, 1603 (m), 1574, 1541, 1520, 1492 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.39 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 3.78 (s, 3H, OMe), 3.84 (2xs, 6H, 2xOCH_3), 6.31 (d, 1H, H-3), 6.68 (d, *J* = 8.4 Hz, 1H, ArH), 6.89 (d, $J_{5,6}$ = 8.3 Hz, 1H, $ArH^{5,6}$), 7.31 (br s., 1H, H-5), 7.45 (br s., 1H, H-8). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.4 (CH_3), 55.0, 59.8, 59.9 (3xOMe), 106.1 (C^5_{arom}), 115.1 (C-3), 116.1 (C-4a), 118.8 (C-8), 119.5 (q, $J_{C,F}$ = 319.1 Hz, CF_3), 119.6 (C^1_{arom}), 124.4 (C-7), 135.2 (C_{arom}), 142.5 (C-8a), 149.9, 150.3, 151.0 (C_{arom}-OMe), 154.0 (C-4 + C-6), 158.8 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ: -73.9. GC-MS (EI, 70 eV): *m/z* (%) = 474 ($[M]^+$,100), 341 (22), 310 (30), 295 (12). HRMS (EI, 70 eV) calcd for $C_{20}H_{17}F_3O_8S$: 474.05907 $[M]^+$; found: 474.05931.

4.1.3.12. 7-(4-*tert*-Butylphenyl)-4-methyl-6-trifluoromethanesulphonyl-2*H*-chromen-2-one (**8l**)

From 4-*tert*-butyl-phenylboronic acid (**6l**) (32 mg). Yield: 52 mg (77%) as a white solid, mp: 131-133 °C. IR (KBr, cm^{-1}): *v* 3070, 2963, 2923, 2851 (w), 1734 (s), 1624, 1609 (m), 1551 (w), 1521, 1494 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.23 (s, 9H, 3xCH_3), 2.40 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 6.31 (d, 1H, H-3), 7.34 (m, 3H, ArH), 7.44 (m., 2H, ArH + H-5), 7.50 (br s., 1H, H-8). ^{13}C NMR (75.47 MHz, $CDCl_3$) δ: 17.5 (CH_3), 30.2 (3xCH_3), 115.2 (C-3), 117.1 (C-5), 118.7 (C-4a + C-8), 119.9 (q, $J_{C,F}$ = 320.4 Hz, CF_3), 124.7, 125.1 (C-7 + C_{arom}), 138.0 (C^1_{arom}), 141.7 (C-8a), 149.9 (C^4_{arom}-CMe_3), 151.3 (C-6), 151.6 (C-4), 158.7 (CO). ^{19}F NMR (282.4, MHz) δ: -73.7. GC-MS (EI, 70 eV): *m/z* (%) = 440 ($[M]^+$, 100), 265 (16),238 (17), 237(85), 209 (34), 165 (32). HRMS (EI,70 eV) calcd for $C_{21}H_{19}F_3O_5S$: 440.08998 $[M]^+$; found: 440.04309.

4.1.4. General procedure of 6-aryl-7-(4-methoxyphenyl)4-methyl-2*H*-chromen-2-one derivatives (**9a-d**)

To a dioxane suspension (3 mL) of bis(triflate) analogue **5** (70 mg, 0.15 mmol), $Pd(PPh_3)$ (5 mg, 3 mol -%, 0.005 mmol), and 4-methoxyphenylboronic acid (**6b**) (28 mg, 0.15 mmol), K_3PO_4 (49 mg, 0.23 mmol) was added. The mixture was heated at 70^{o}C under Argon atmosphere. After 6 h, a dioxan (3 mL) suspension of arylboronic acid **6c,g,j,a** (0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol-%, 0.005 mmol), K_3PO_4 (49 mg, 0.23 mmol) was added. The mixture was heated at 120 ^{o}C under Argon atmosphere for 6 h. The reaction mixture was worked up as experiments **7a-e**.

4.1.4.1. 6-(4-Chlorophenyl)-7-(4-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (**9a**)

From 4-chlorophenylboronic acid (**6c**) (28 mg). Yield: 42 mg (73%) as a white solid, mp: 172-174 °C. IR (KBr, cm^{-1}): *v* 3115, 3092, 3076, 2966, 2932, 2845 (w), 1731 (s), 1620, 1600 (m), 1580, 1540, 1522, 1493 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.39 (d, 3H, $J_{CH3,H3}$ = 1.1 Hz, CH_3), 3.73 (s,

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3H, OMe), 6.24 (d, 1H, H-3), 6.72 (d, 2H, *J* = 8.1 Hz, ArH), 6.95-6.99 (m, 4H, ArH), 7.26 (m, 2H, ArH + H-8), 7.46 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (CH_3), 54.2 (OMe), 112.7 (C-3), 114.1 (C_{arom}), 117.4 (C-8), 117.8 (C-4a), 125.3, 127.4, 129.8, 130.0 (C_{arom}), 130.5 (C-5), 132.0 (C-6), 134.7 (C_{arom}-Cl), 137.8, 143.1 (C-7 + C_{arom}), 151.0 (C-8a), 151.9 (C-4), 158.1 (C_{arom}-OMe), 159.7 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 376 ([M]$^+$, [^{35}Cl], 100), 348 (13). HRMS (EI, 70 eV) calcd for $C_{23}H_{17}{}^{35}ClO_3$: 376.08607 ([M]$^+$); found 367.08589.

4.1.4.2. 6-(4-Fluorophenyl)-7-(4-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (**9b**)

From 4-fluorophenylboronic acid (**6f**) (25 mg). Yield: 43 mg (78%) as a white solid, mp: 192-194 °C. IR (KBr, cm^{-1}): *v* 3115, 3092, 3076, 2966, 2932, 2845 (w), 1731 (s), 1620, 1600 (m), 1580, 1540, 1522, 1493 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.39 (d, 3H, $J_{CH3,H3}$ = 1.3 Hz, CH_3), 3.72 (s, 3H, OMe), 6.24 (d, 1H, H-3), 6.70 (d, 2H, *J* = 8.4 Hz, ArH), 6.88-7.03 (m, 6H, ArH), 7.28 (br s., 1H, H-8), 7.46 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (CH_3), 54.2 (OMe), 112.7 (C-3), 114.2 (C_{arom}) 117.3 (C-8 + C-4a), 117.7 (d, *J* = 8.2 Hz, C_{arom}), 125.3 (C_{arom}), 129.8 (C-5), 130.6 (d, *J* = 21.6 Hz, C_{arom}), 134.9 (C-7), 135.4 (C-6), 143.1 (C_{arom}), 151.0 (C-8a), 151.8 (C-4), 158.7 (q, $J_{C,F}$ = 273.1 Hz, C_{arom}-F), 159.8 (C_{arom}-OMe), 162.5 (CO). ^{19}F NMR (282 MHz, $CDCl_3$) δ:-115.3. GC-MS (EI,70 eV): *m/z* (%) = 360 ([M]$^+$, 100), 348 (13). HRMS (EI, 70 eV) calcd for $C_{23}H_{17}FO_3$: 360.11562 [M]$^+$; found: 360.11580.

4.1.4.3. 7-(4-Methoxyphenyl)-4-methyl-6-(3-methylphenyl)-2*H*-chromen-2-one (**9c**)

From 3-methylphenylboronic acid (**6i**) (25 mg). Yield: 41 mg (75%) as a white solid, mp 209-211 °C. IR (KBr, cm^{-1}): *v* 3111, 3094, 3077, 2967, 2931, 2846 (w), 1732 (s),1624, 1606 (m), 1583,1547, 1526, 1495 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.21 (s, 3H, CH_3), 2.37 (d, 3H, $J_{CH3,H3}$ = 1.2 Hz, CH_3), 3.69 (s, 3H, OMe), 6.21 (d, 1H, H-3), 6.70 (d, 2H, *J* = 8.4 Hz, ArH), 6.81 (d, 2H, *J* = 8.9 Hz, ArH), 6.93-7.06 (m, 3H, ArH), 7.27 (br s., 1H, H-8), 7.48 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6, 20.3 (2xCH_3), 54.1 (OMe), 112.5 (C-3), 113.8 (C_{arom}), 117.1 (C-8), 117.6 (C4a), 125.9, 126.6, 126.9, 129.3 ($_{Carom}$), 129.7 (C-5), 131.0 (C-6), 136.8 (C-7), 139.3, 143.1 (C_{arom}), 151.2 (C-8a), 151.6 (C-4), 158.0 (C_{arom}-OMe), 159.9 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 356 ([M]$^+$, 100), 341(10). HRMS (EI, 70 eV) calcd for $C_{24}H_{20}O_3$: 356.14070 [M]$^+$; found: 356.14106.

4.1.4.4. 6-(3,5-Dimethlyphenyl)-7-(4-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (**9d**)

From 3,5-dimethylphenylboronic acid (**6a**) (28 mg). Yield: 46 mg (81%) as a white solid, mp: 203-205 °C. IR (KBr, cm^{-1}): *v* 3117, 3094, 3078, 2969, 2934, 2847 (w), 1734 (s), 1627, 1609 (m), 1585, 1549, 1528, 1497 (w). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.15 (6H, 2xCH_3), 2.38 (d, 3H, $J_{CH3,H3}$ = 1.4 Hz, CH_3), 3.71 (s, 3H, OMe), 6.22 (d, 1H, H-3), 6.67-6.79 (m, 5H, ArH), 6.99 (d,

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2H, *J* = 8.4 Hz, ArH), 7.28 (br s., 1H, H-8), 7.47 (br s., 1H, H-5). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 17.6 (2xCH_3), 21.6 (CH_3), 54.2 (OMe), 113.8 (C-3), 114.1 (C_{arom}), 117.1 (C-8), 117.5 (C-4a), 125.3, 126.4, 126.6, 127.5 (C_{arom}), 129.7 (C-5), 131.0 (C-6), 136.2 (C-7), 136.5, 136.6, 139.2, 143.1 (C_{arom}), 151.2 (C-8a), 151.6 (C-4), 157.9 (C_{arom}-OMe), 159.9 (CO). GC-MS (EI, 70 eV): *m/z* (%) = 370 ($[M]^+$,100), 355 (12), 300 (11). HRMS (EI, 70 eV) calcd for $C_{25}H_{22}O_3$: 370.15635 $[M]^+$; found: 370.15622.

4.1.5. 3-Bromo-6,7-dihydroxy-4-methyl-2*H*-chromen-2-one (**10**)

To a solution of 4-methyl-6,7-dihydroxycoumarin (**4**) (1.0 equiv., 0.003 mol, 0.50 g) in glacial acetic acid (20 mL) bromine (2.0 equiv., 0.005 mol, 0.80 g) were added dropwise under argon atmosphere, the reaction mixture was stirred at 30 °C for 2 h, the reaction monitored by TLC (heptane / EtOAc = 9.5 : 0.5). The reaction mixture poured onto ice-cold water (250 mL), stirred with a solution of sodium hydrogen sulphite till the yellow color disappeared, filtered and the residue was purified by column chromatography (silica gel, heptane / EtOAc = 10 : 1) to give **10** as a yellow solid (0.52 g, 75%), mp: 181-183 ^{o}C. NMR (300 MHz, $CDCl_3$) δ: 2.50 (s, 3H, CH_3), 6.77 (s, 1H, ArH), 7.09 (s, 1H, ArH), 9.80 (s, 1H, OH), 10.30 (s, 1H, OH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 19.4 (CH_3), 102.4 (CH), 107.6 (C), 109.9 (CH), 111.2, 143.3, 146.1, 150.5 (C), 161.3 (CO). IR (KBr, cm^{-1}): *v* 3057, 2995, 2950, 2930, 2831 (w), 1599 (s), 1574, 1551 (w). GC-MS (EI, 70 eV): *m/z* (%) 272 ($[M+H]^+$, [^{81}Br], 100), 271 ($[M]^+$, [^{81}Br], 26), 270 ($[M+H]^+$, [^{79}Br], 99), 269 ($[M]^+$, [^{79}Br], 10), 244 (20), 242 (22), 192 (12), 191 (17),164 (58), 89 (16). HRMS (EI, 70 eV) calcd for $C_{10}H_8{}^{81}BrO_4$ $[M+H]^+$: 272.9581, found: 272.9574, $C_{10}H_8{}^{79}BrO_4$ $[M+H]^+$: 270.96005; found: 270.95949.

4.1.6. 3-Bromo-4-methyl-2-oxo-2*H*-chromene-6,7-diyl bis-(trifluoromethanesulfonate) (**11**)

To a solution of **10** (0.50 g, 2.60 mmol) in CH_2Cl_2 (30 mL) was added triethylamine (0.36 mL, 10.4 mmol) at room temperature under an argon atmosphere. After 10 min, Tf_2O (1.0 mL, 6.20 mmol) was added at -78°C. The mixture was allowed to warm to 20 °C and stirred for 6 h. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography (flash silica gel, heptane / EtOAc = 4 : 1) without aqueous work up to give **11** as a white solid (0.90 g, 75%), mp: 125-27 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.58 (CH_3), 7.45 (s , 1H, ArH), 7.79 (s, 1H, ArH). ^{13}C NMR (75.46 MHz, $CDCl_3$) δ: 18.80 (CH_3), 111.6 (CH), 115.2 (C), 115.5 (q, $J_{F,C}$ = 316.0 Hz, CF_3), 118.9 (C), 119.2 (CH), 120.3 (q, $J_{F,C}$ = 316.0 Hz, CF_3), 135.9, 140.6, 147.6, 149.7 (C), 153.9 (CO). ^{19}F NMR (282.4, MHz) δ: -72.7, -72.9 (3F, CF_3). IR (KBr, cm^{-1}): *v* 3123, 3051, 2962, 2925 (w), 1742 (s), 1670, 1621, 1612, 1571 (w), 1492 (m). GC-MS (EI, 70 eV): *m/z* (%) = 535 ($[M]^+$, [^{81}Br], 19), 533 ($[M]^+$, [^{79}Br], 17), 403 (27), 401 (24), 311 (28), 281 (11), 309

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(29), 202 (13), 77 (25). HRMS (EI, 70 eV) calcd for $C_{12}H_5O_8{}^{81}BrF_6S_2$ $[M]^+$: 535.84875; found: 535.84860, $C_{12}H_5O_8{}^{79}BrF_6S_2$ $[M]^+$: 533.85079; found: 533.85079.

4.1.7. General procedure for synthesis of 3,6,7-tris(aryl)-4-methyl-2*H*-chromen-2-one derivatives (**12a-c** and **12e-p**)

The reactions were carried out in a pressure tube. A 1,4-dioxane solution (4 mL) of **11** (70 mg, 0.13 mmol), arylboronic acid (3.1 equiv., 0.41 mmol), aqueous K_2CO_3 (2 M, 2 mL), and $Pd(PPh_3)_4$ (14 mg, 9 mol-%, 0.012 mmol) was heated at 120 °C for 10 h under argon atmosphere. After cooling to 20 °C, water was added and the reaction mixture was extracted with CH_2Cl_2 (3 x 25 mL). The organic layers were dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (silica gel, heptane/EtOAc = 9:1).

4.1.7.1. 3,6,7-Tris(3,5-dimethylphenyl)-4-methyl-2*H*-chromen-2-one (**12a**)

From 3,5-dimethylphenylboronic acid (**6a**) (61 mg). Yield: 43 mg (70%) as a white solid, mp: 190-192 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.13 (s, 6H, 2xCH_3), 2.14 (s, 6H, 2xCH_3), 2.24 (s, 3H, CH_3), 2.28 (s, 6H, 2xCH_3), 6.68 - 6.69 (m, 5H, ArH), 6.79 - 6.84 (m, 5H, ArH), 6.94 (d, J = 8.6, Hz, 1H, ArH), 7.32 (s, 1H, ArH). 7.55 (br. s, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.5 (2xCH_3), 20.2 (2xCH_3), 20.3 (2xCH_3), 28.6 (CH_3), 116.9 (CH), 118.3 (C), 125.6, 126.4, 126.5, 126.6, 127.3, 127.8, 127.9 (CH), 133.4, 136.3, 136.3, 136.8, 138.6, 139.3, 143.1, 143.1, 143.2, 146.3, 147.4, 150.6, 154.2 (C),161.2 (CO). IR (KBr, cm^{-1}): ν 3012, 2955 (w), 2919 (m), 2853 (w), 1707 (s), 1610, 1597 (m), 1552, 1495 (w). GC - MS (EI, 70 eV): *m/z* (%) = 472 ($[M]^+$, 100), 444 (15), 429 (12), 214 (14), 179 (10). HRMS (EI, 70 eV) calcd for $C_{34}H_{32}O_2$ $[M]^+$: 472.240; found: 472.24014.

4.1.7.2. 3,6,7-Tris(4-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (**12b**)

From 4-methoxyphenylboronic acid (**6b**) (61 mg). Yield: (50 mg, 80%) as a white solid, mp: 169-170 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.28 (s, 3H, CH_3), 3.72 (s, 6H, 2xOMe), 3.78 (s, 3H, OMe), 6.73 (dd, J = 1.7, 8.3 Hz, 4H, ArH), 6.93 (d, J = 8.6, Hz, 2H, ArH), 6.99 (dd, J = 1.6, 8.6 Hz, 4H, ArH), 7.23 (d, J = 8.6, Hz, 2H, ArH), 7.30 (s, 1H, ArH), 7.53 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 16.6 (CH_3), 55.2, 55.3, 55.5 (OMe), 113.6, 113.8, 117.9, 119.4, 126.6 (CH), 126.7, 126.9 (C), 130.8, 130.9, 131.3, 131.6 (CH),132.2, 132.9, 136.6, 143.4, 147.1, 151.6, 158.6, 158.9, 159.4 (C), 161.3 (CO). IR (KBr, cm^{-1}): ν 3059, 2993, 2952, 2931, 2834 (w), 1715, 1599 (s), 1574, 1551 (w). GC-MS (EI, 70 eV): *m/z* (%) = 478 ($[M]^+$, 100), 450 (14), 207 (13). HRMS (EI, 70 eV) calcd for $C_{31}H_{26}O_5$ $[M]^+$: 478.53514; found: 478.53412.

4.1.7.3. 3,6,7-Tris(4-chlorophenyl)-4-methyl-2*H*-chromen-2-one (**12c**)

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From 4-chlorophenylboronic acid (**6c**) (61 mg). Yield: 39 mg (61%) as a white solid, mp: 200-201 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.28 (s, 3H, CH_3), 6.97 - 7.02 (m, 3H, ArH), 7.14 - 7.21 (m, 5H, ArH), 7.27 - 7.40 (m, 6H, ArH) .^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 16.6 (CH_3), 114.1, 114.2, 114.3, 115.2, 117.8, 119.3 (CH), 124.4 (C), 124.7, 124.8 (CH), 128.7, 128.8, 130.3, 132.0, 132.8, 134.6, 143.4, 145.2, 150.5, 151.5, 156.9 (C), 160.4 (CO). IR (KBr, cm^{-1}): *v* 3067, 3032, 2979, 2927, 2918, 2888, 2839 (w), 1715, 1599 (s), 1572, 1548, 1519 (w), 1512 (m). GC-MS (EI, 70 eV): *m/z* (%) = GC - MS (EI, 70 eV): *m/z* (%) = 490 ([M]$^{+}$, 3×[^{35}Cl], 99), 345 (45), 270 (15). HRMS (EI, 70 eV) calcd for $C_{28}H_{17}{}^{35}Cl_3O_2$ [M]$^{+}$: 490.02886; found: 490.02834.

4.1.7.4. 3,6,7-Tris(4-ethoxyphenyl)-4-methyl-2*H*-chromen-2-one (12e)

From 4-ethoxyphenylboronic acid (**6e**) (68 mg). Yield: 57 mg (84%) as a white solid (57 mg, 84 %), mp: 179-180 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.30 - 1.35 (m, 9H, 3xCH_3), 2.26 (s, 3H, CH_3), 3.91 - 3.98 (m, 6H, 3xOCH_2), 6.67 - 6.72 (m, 4H, ArH), 6.88 (d, *J* = 8.6, Hz, 2H, ArH), 6.97 (dd, *J* = 1.9, 8.6 Hz, 4H, ArH), 7.15 (d, *J* = 8.6, Hz, 3H, ArH), 7.53 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 14.7, 14.8, 14.9, 16.6 (CH_3), 63.4, 63.5, 63.6 (OCH_2), 113.1, 113.2, 113.3, 114.2, 116.8, 118.3 (CH), 125.4 (C), 125.7, 125.8 (CH), 129.7, 129.8, 130.3, 131.0, 131.8, 135.6, 142.4, 146.2, 150.5, 150.5, 156.9 (C), 160.4 (CO). IR (KBr, cm^{-1}): *v* 3066, 3031, 2978, 2928, 2919, 2887, 2849 (w), 1716, 1599 (s), 1573, 1548, 1519 (w), 1510 (m). GC-MS (EI, 70 eV): *m/z* (%) = 520 ([M]$^{+}$, 100), 492 (14), 209 (13). HRMS (EI, 70 eV) calcd for $C_{34}H_{32}O_5$ [M]$^{+}$: 520.22497; found: 520.22478.

4.1.7.5. 3,6,7-Tris(4-fluorophenyl)-4-methyl-2*H*-chromen-2-one (12f)

From 4-fluorophenylboronic acid (**6f**) (59 mg). Yield: 40 mg (70%) as a white solid, mp: 222-224°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.28 (s, 3H, CH_3) , 6.86 - 6.92 (m, 4H, ArH), 7.00 - 7.04 (m, 4H, ArH), 7.12 (d, *J* = 8.52 Hz, 2H, ArH), 7.21 - 7.26 (m, 2H, ArH), 7.32 (s, 1H, ArH), 7.56 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 15.6 (CH_3), 114.1 (d, $J_{F,C}$ = 21.4 Hz), 114.4 (d, $J_{F,C}$ = 21.4 Hz), 115.6 (d, $J_{F,C}$ = 21.4 Hz), 117.2 (CH), 118.6, 125.6 (C), 126.0 (CH), 129.1 (d, $J_{F,C}$ = 3.5 Hz) (C), 130.2, 130.3 (CH), 130.4 (C), 130.8 (d, $J_{F,C}$ = 1.7 Hz) (CH), 142.0, 146.5, 150,9, 159.3, 159.6, 159.7 (C), 159.9 (d, $J_{F,C}$ = 246.9 Hz)(CF), 162.6 (d, $J_{F,C}$ = 246.0 Hz) (CF), 162.9 (d, $J_{F,C}$ = 247.4 Hz)(CF), 163.2 (CO). ^{19}F NMR (282.4, MHz) δ: -113.1, -144.8, -114.9 (ArF). IR (KBr, cm^{-1}): *v* 3038, 2929, 2859, 1892 (w), 1604 (m), 1558 (w), 1507 (s), 1490 (m). GC-MS (EI, 70 eV): *m/z* (%) = 442 ([M]$^{+}$, 100), 441 (21), 415 (10), 414 (38), 413 (20). HRMS (EST-TOF/MS): calcd for. $C_{28}H_{17}O_2F_3$ [M]$^{+}$: 442.11752; found: 442.11697.

4.1.7.6. 4-Methyl-3,6,7-tris[4-(trifluoromethyl)phenyl]-2*H*-chromen-2-one (12g)

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From 4-(trifluoromethyl)phenylboronic acid (**6g**) (77 mg). Yield: 49 mg (63%) as a white solid, mp: 188-189 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.30 (s, 3H, CH_3) , 6.52 - 6.59 (m, 5H, ArH), 7.00 - 7.06 (m, 3H, ArH), 7.14 (d, J = 8.52 Hz, 2H, ArH), 7.23 - 7.27 (m, 2H, ArH), 7.30 (s, 1H, ArH), 7.53 (s, 1H, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$) δ: 16.6 (CH_3), 115.1 (d, $J_{F,C}$ = 21.4 Hz), 115.4 (d, $J_{F,C}$ = 21.4 Hz), 115.6 (d, $J_{F,C}$ = 21.4 Hz), 117.3 (CH), 118.7, 125.8 (C), 126.2 (CH), 129.4 (d, $J_{F,C}$ = 3.5 Hz) (C), 130.1, 130.3 (CH), 130.4 (C), 130.9 (d, $J_{F,C}$ = 1.7 Hz) (CH), 133.2 (d, $J_{F,C}$ = 3.6 Hz), 142.1, 146.6 (d, $J_{F,C}$ = 3.3 Hz), 150. 9, 159.2, 159.5, 159.6, 159.8 (C), 159.9 (d, $J_{F,C}$ = 246.9 Hz) (CF_3), 162.7 (d, $J_{F,C}$ = 246.0 Hz) (CF_3), 162.9 (d, $J_{F,C}$ = 247.4 Hz) (CF_3), 163.3 (CO). ^{19}F NMR (282.4, MHz) δ: - 62.5, - 62.6, - 62.7(3F,CF_3). IR (KBr, cm^{-1}): v 3069, 2959, 2921, 2850 (w), 1721 (s), 1650, 1645, 1615, 1575, 1556, 1486, 1463, 1455 (w) . GC-MS (EI, 70 eV): m/z (%) = 592 ([M]$^+$, 100), 591 (45), 573 (13), 565 (11), 564 (37), 563 (18), 419 (15). HRMS (EST-TOF/MS): calcd for. $C_{31}H_{17}O_2F_9$ [M]$^+$: 592.10794; found: 592.10714.

4.1.7.7. 4-Methyl-3,6,7-tri-*p*-tolyl-2*H*-chromen-2-one (12h)

From 4-methylphenylboronic acid (**6h**) (55 mg). Yield: 42 mg (75%) as a white solid, mp: 163-165 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.09 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 6.99 (br. s, 1H, ArH) 7.12 (d, J = 8.3, Hz, 2H, ArH), 7.18 - 7.23 (m, 5H, ArH), 7.28 - 7.34 (m, 2H, ArH), 7.55 (s, 2H, ArH), 7.64 (br. s, 2H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.2, 16.3, 20.1, 20.3 (CH_3), 28.5 (C), 117.2, 118.1, 118.2 (CH), 118.5 (C), 125.6, 125.9, 126.1, 126.4, 126.3 (CH), 129.4, 133.2, 136.1, 136.3, 137.0, 138.5, 139.4, 143.2, 146.2, 150.6 (C), 160.3 (CO). IR (KBr, cm^{-1}): v = 2962, 2923, 2854 (w), 1715 (s), 1608 (m), 1586, 1551, 1479 (w). GC-MS (EI, 70 eV): m/z (%) = 430 ([M]$^+$, 100), 420 (22), 413 (13), 186 (18). HRMS (EI, 70 eV) calcd for $C_{31}H_{26}O_2$ [M]$^+$: 430.19328; found: 430.19355.

4.1.7.8. 4-Methyl-3,6,7-tri-*m*-tolyl-2*H*-chromen-2-one (12i)

From 3-methylphenylboronic acid (**6i**) (55 mg). Yield: 39 mg, 70%) as a white solid, mp: 143-145 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.20 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 6.83 (br. s, 2H, ArH) 6.94 - 7.06 (m, 6H, ArH), 7.15 (t, J = 7.3, Hz, 2H, ArH), 7.25 (t, J = 7.2, Hz, 2H, ArH), 7.35 (s, 1H, ArH), 7.58 (br. s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: = 15.6, 16.6, 20.4, 20.5 (CH_3), 28.6 (C), 117.1, 118.2, 118.3 (CH), 118.4 (C), 125.8, 125.9, 126.0, 126.5, 126.6, 126,8, 127.0, 127.3, 127.9, 129.3, 129.4 (CH),129.5, 133.4, 136.2, 136.6, 137.0, 138.6, 139.3, 143.1, 146.3, 150.7 (C), 160.2 (CO). IR (KBr, cm^{-1}): v = 2961, 2920, 2853 (w), 1711 (s), 1607 (m), 1585, 1552, 1478 (w). GC-MS (EI, 70 eV): m/z (%) = 430 ([M]$^+$, 100), 429 (21), 415 (10), 402 (18), 186 (10). HRMS (EI, 70 eV) calcd for $C_{31}H_{26}O_2$ [M]$^+$: 430.19328; found: 430.19373.

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4.1.7.9. 3,6,7-Tris(3-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (12j)

From 3-methoxyphenylphenylboronic acid (**6j**) (62 mg). Yield: 50 mg (80%) as a white solid, mp: 101-103 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.27 (s, 3H, CH_3), 3.57 (s, 6H, 2x OCH_3), 3.76 (s, 3H, OCH_3), 6.60 - 6.62 (m, 3H, ArH), 6.68 - 6.74 (m, 3H, ArH), 6.78 - 6.81(m, 3H, ArH), 7.10 (d, J = 8.6, Hz, 1H, ArH), 7.17 (d, J = 8.4, Hz, 1H, ArH), 7.28 - 7.37 (m, 2H, ArH), 7.61 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 16.6 (CH_3), 55.1, 55.2, 55.3 (OCH_3), 112.7, 113.5, 113.7, 115.0, 115.4, 115.7, 118.1 (CH), 119.6 (C), 122.0, 122.2, 122.3, 126.9 (CH), 127.7 (C), 129.2, 129.3, 129.5 (CH), 136.4, 136.9, 141.4, 141.7, 143.8, 147.5, 151.9, 159.2, 159.3, 159.5 (C), 160.8 (CO). IR (KBr, cm^{-1}): v 3054, 2998, 2952, 2934, 2823 (w), 1712, 1598, 1575, (s), 1556 (m),1477 (w). GC - MS (EI, 70 eV): m/z (%) = 478 ([M]$^{+}$, 100), 477 (22), 207 (13). HRMS (EI, 70 eV) calcd for $C_{31}H_{26}O_5$ [M]$^{+}$: 478.17748; found: 478.17709.

4.1.7.10. 4-Methyl-3,6,7-tris(2,3,4-trimethoxyphenyl)-2*H*-chromen-2-one (12k)

From 2,3,4-trimethoxyphenylboronic acid (**6k**) (86 mg). Yield: 69 mg (80%) as a white solid, mp: 110-112 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.20 (s, 3H, CH_3), 3.63 (s, 9H, 3xOCH_3), 3.66 (s, 9H, 3xOCH_3), 3.85 (s, 9H, 3xOCH_3), 6.99 (dd, J = 1.9, 8.4 Hz, 2H, ArH), 6.62 - 6.70 (m, 3H, ArH), 6.18 (d, J = 8.3 Hz, 1H, ArH), 7.34 (s, 1H, ArH), 7.59 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.5 (CH_3), 28.6 (3xOCH_3), 54.9 (3xOCH_3), 55.0 (3xOCH_3), 105.3, 105.4, 106.3, 108.3, 108.4, 112.2, 112.4, 117.2 (CH), 120.3, 122.7, 124.2, 124.3, 124.7, 125.7, 126.0, 133.3, 140.5, 140.8, 140.9, 141.3, 147.8, 150.1, 150.3, 150.9, 152.0, 152.2, 153.0 (C), 160.2 (CO). IR (KBr, cm^{-1}) : v 3065, 3034 (w), 2971 (m), 2931, 2920, 2881, 1887 (w), 1721, 1600 (s), 1573, 1557, 1552, 1518, 1506, 1485 (w). GC-MS (EI, 70 eV): m/z (%) = 658 ([M]$^{+}$, 100), 620 (10), 577 (20), 438 (17), 411 (25), 207 (14). HRMS (EI, 70 eV) calcd for $C_{37}H_{38}O_{11}$ [M]$^{+}$: 658.24141; found: 658.24135.

4.1.7.11. 3,6,7-Tris(4-*tert*-butylphenyl)-4-methyl-2*H*-chromen-2-one (12l)

From 4-*tert*-butylphenylboronic acid (**6l**) (72 mg). Yield: 45 mg (62%) as a white solid, mp: 150-152 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22 (s, 9H, 3xCH_3), 1.23 (s, 9H, 3xCH_3), 1.28 (s, 9H, 3xCH_3), 2.27 (s, 3H, CH_3), 7.01 (d, J = 8.3, Hz , 4H, ArH), 7.16 - 7.20 (m, 7H, ArH), 7.38 (t, J = 7.2, Hz, 3H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.7 (CH_3), 30.2 (3xCH_3), 30.3 (3xCH_3), 30.4 (3xCH_3), 33.4, 33.5, 33.6, 117.0 (C), 118.4, 123.8, 123.8, 124.2 (CH), 125.9, 126.1 (C), 128.3, 128.4, 128.7 130.4 (CH),135.7, 136.0, 136.5, 142.9, 146.3, 148.8, 149.3, 149.9, 150.6 (C), 160.2 (CO). IR (KBr, cm^{-1}): v 3030 (w), 2959 (s), 2903, 2865 (w), 1719 (s), 1609, 1604, 1564, 1557, 1547, 1505 (w). GC-MS (EI, 70 eV): m/z (%) = 556 ([M]$^{+}$, 100), 542 (18), 541 (49), 385 (11), 251

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(18), 149 (18), 71 (10). HRMS (EI, 70 eV) calcd for $C_{40}H_{44}O_2$ $[M]^+$: 556.33358; found: 556.33339.

4.1.7.12. 3,6,7-Tris(3,4-dimethylphenyl)-4-methyl-2*H*-chromen-2-one (12m)

From 3,4-dimethylphenylboronic acid (**6m**) (61 mg). Yield: 37 g (60%) as a white solid, mp: 171-172 ^oC. ^1H NMR (300 MHz, $CDCl_3$) δ: 2.11 (s, 3H, CH_3), 2.13 (s, 6H, 2xCH_3), 2.16 (s, 6H, 2xCH_3), 2.23 (s, 6H, 2xCH_3), 6.75 (br. s, 2H, ArH) 6.87 - 7.01 (m, 5H, ArH), 7.16 (t, J = 7.4, Hz, 2H, ArH), 7.31 (s, 1H, ArH), 7.53 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.5 (2xCH_3), 18.3 (2xCH_3), 18.6 (2xCH_3), 18.7 (CH_3), 28.6 (C), 117.1 (CH), 118.3 (C), 125.9, 126.1, 126.2, 126.3, 126.4, 128.2, 128.6, 129.7, 129.8, 1390.0 (CH), 131.2, 134.1, 134.6, 135.2, 135.3, 135.5, 135.6, 136.0, 126.3, 137.1, 142.9, 146.2, 149.5 (C), 160.3 (CO). IR (KBr, cm^{-1}): v 2961, 2919, 2854 (w), 1713 (s), 1609 (m), 1573, 1568, 1549, 1503, 1484 (w). GC-MS (EI, 70 eV): *m/z* (%) = 472 ($[M]^+$, 100), 471 (26), 457 (10), 445 (17), 443 (11), 429 (13), 414 (11), 207 (16). HRMS (EI, 70 eV) calcd for $C_{34}H_{32}O_2$ $[M]^+$: 472.23968; found: 472.23921.

4.1.7.13. 3,6,7-Tris(4-isopropylphenyl)-4-methyl-2*H*-chromen-2-one (12n)

From 4-isopropylphenylboronic acid (**6n**) (66 mg). Yield: 47 mg (70%) as a white solid, mp: 120-122 ^oC. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.14 (s, 6H, 2xCH_3), 1.16 (s, 6H, 2xCH_3), 1.22 (s, 6H, 2xCH_3), 2.25 (s, H, CH_3), 2.27 - 2.91 (m, 3H, 3xCH), 6.96 - 7.01 (m, 8H, ArH), 7.15 (d, J = 8.4, Hz, 2H, ArH), 7.24 (d, J = 8.2, Hz, 2H, ArH), 7.33 (s, 1H, ArH), 7.56 (s, 1H, ArH).^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.6 (2xCH_3), 22.8 (2xCH_3), 22.9 (2xCH_3), 24.7 (CH_3), 32.6, 32.7, 32,9 (CH), 117.0 (C), 118.4, 124.7 (CH), 125.0, 125.4 (C), 126.0, 126.1, 128.3, 128.5, 128.9, 130.7 (CH) 136.1, 136.2, 136.9, 142.9, 146.3, 146.5, 147.1, 147.6, 150.6 (C), 160.3 (CO). IR (KBr, cm^{-1}): v 3064, 3041, 3024 (w), 2957 (s), 2924, 2865 (w), 1724 (s), 1613, 1604 (m), 1568, 1551, 1510, 1506, 1484 (w). GC-MS (EI, 70 eV): *m/z* (%) = 514 ($[M]^+$, 100), 500 (10), 499 (17),

4.1.7.14. 3,6,7-Tris(4-isopropoxyphenyl)-4-methyl-2*H*-chromen-2-one (12o)

From 4-isopropoxyphenylboronic acid (**6o**) (73 mg). Yield: 57 mg (77%) as a white solid, mp: 210-211 ^oC. ^1H NMR (300 MHz, $CDCl_3$) δ: 1.28 (q, J = 7.4 Hz, 18H, 6xCH_3), 2.28 (s, 3H, CH_3), 4.38 - 4.59 (m, 3H, 3xOCH), 6.64 - 6.72 (m, 4H, ArH), 6.97 (d, J = 8.4 Hz, 3H, ArH), 6.99 (dd, J = 1.7, 8.2 Hz, 4H, ArH), 7.18 (d, J = 8.3 Hz, 2H, ArH), 7.30 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.6 (2xCH_3), 21.0 (2xCH_3), 21.1 (2xCH_3), 23.7 (CH_3), 67.2, 68.8, 68.8 (OCH), 114.4, 114.5, 114.6, 116.8, 118.3 (CH), 125.3, 125.7 (C), 129.8, 129.9, 130.4 (CH), 130.9, 131.7, 135.6, 142.4, 146.1, 150.5, 150.6, 155.8, 156.2, 156.7 (C), 160.4 (CO). IR (KBr, cm^{-1}) : v 3062, 3030, 2970,

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2920, 2851 (w), 1721 (s), 1650, 1644, 1633 (w), 1599 (m), 1573 (w), 1518, 1506, 1484, 1463, 1455 (w). GC-MS (EI, 70 eV): *m/z* (%) = 562 ([M]$^+$, 100), 520 (10), 478 (10), 473 (27), 436 (93), 435 (19), 408 (24), 407 (14). HRMS (EI, 70 eV) calcd for $C_{37}H_{38}O_2$ [M]$^+$: 562.27138; found: 562.27101.

4.1.7.15. 3,6,7-Tris(4-ethylphenyl)-4-methyl-2*H*-chromen-2-one (**12p**)

From 4-ethylphenylboronic acid (**6p**) (61 mg). Yield: 46 mg (75%) as a white solid, mp: 134-135 ^oC.^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.11 - 1.23 (m, 9H, 3xCH_3), 2.26 (s, 3H, CH_3), 2.50 - 2.61 (m, 6H, 3xCH_2), 6.68 - 6.71 (m, 4H, ArH), 6.77 (d, *J* = 8.6, Hz, 2H, ArH), 6.87 (dd, *J* = 1.6, 8.6 Hz, 4H, ArH), 7.13 (d, *J* = 8.6, Hz, 3H, ArH), 7.51 (s, 1H, ArH). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 15.3, 15.4, 15.5, 16.6 (CH_3), 28.4, 28.6, 28.7 (CH_2), 118.1, 119.5, 127.1 (CH), 127.2, 127.6 (C), 127.9, 129.6, 129.7, 130.1, 131.7 (CH), 137.0, 137.1, 137.8, 142.9, 143.4, 143.9, 144.2, 147.3, 151.7, 152.8, (C), 161.2 (CO). IR (KBr, cm^{-1}): *v* 3407, 3071, 3024, 2962, 2927, 2871, 2854 (w), 1722 (s), 1613, 1604 (m), 1573, 1568, 1556, 1552 (w). GC-MS (EI, 70 eV): *m/z* (%) = 472 ([M]$^+$, 100), 444 (13), 443 (12). HRMS (EI, 70 eV) calcd for $C_{34}H_{32}O_2$ [M]$^+$: 472.23968; found: 472.23912.

4.2. Crystal structure determination of 5, 7e and 8b. Data were collected on a Bruker APEX II Duo diffractometer.The structure was solved by Direct Methods andrefined by full-matrix least-squares procedures on *F*2 withthe SHELXTL software package [-]. Hydrogen atoms wereplaced in idealized positions and included as constrainedinto the refinement while all other atoms were refined withanisotropic displacement parameters.

4.3. *In vitro* anti-HIV assay. Evaluation of the antiviral activity of the compounds 6-15 and 16-19 against HIV-1 strain III_B and HIV-2 strain (ROD) in MT-4 cells was performed using the MTT assay as previously described[39,40]. Briefly, stock solutions (10 x final concentration) of test compounds were added in 25 µL volumes to two series of triplicate wells so as to allow simultaneous evaluation of their effects on mock-and HIV-infected cells at the beginning of each experiment. Serial 5-fold dilutions of test compounds were made directly in flat-bottomed 96-well microtiter trays using a Biomek 3000 robot (Beckman instruments). Untreated control HIV-and mock-infected cell samples were included for each sample. HIV-1(III_B)[43] or HIV-2 (ROD)[44] stock (50 µL) at 100-300 $CCID_{50}$ (50% cell culture infectious dose) or culture medium was added to either the infected or mock-infected wells of the microtiter tray. Mock-infected cells were used to evaluate the effect of test compound on uninfected cells in order to assess the cytotoxicity of the test compound. Exponentially growing MT-4 cells[45] were centrifuged for 5 min at 1,000 rpm and the supernatant was discarded. The MT-4 cells were resuspended at 6 x 10^5 cells/mL and 50 µL

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volumes were transferred to the microtiter tray wells. Five days after infection, the viability of mock-and HIV-infected cells was examined spectrophotometrically by the MTT assay.

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46. CCDC-xxx contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Graphical Abstract

Synthesis of arylated coumarins by Suzuki-Miyaura cross-coupling. Reactions and anti-HIV activity

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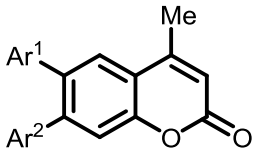

	IC_{50} against HIV-1 (III_B)	
7a: $Ar^1 = Ar^2 = 3,5\text{-}(Me)_2C_6H_3$	4.57 µM	SI = 3
8i: $Ar^1 = OTf$, $Ar^2 = 3\text{-}MeC_6H_5$	13.20 µM	SI = 5
8k: $Ar^1 = OTf$, $Ar^2 = 2,3,4\text{-}(MeO)_3C_6H_5$	0.50 µM	SI < 1
9d: $Ar^1 = 4\text{-}MeO\text{-}C_6H_4$, $Ar^2 = 3,5\text{-}(Me)_2C_6H_3$	0.45 µM	SI < 1

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