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Synthesis of arylated xanthones by site-selective Suzuki–Miyaura reactions of the bis(triflate) of 1,3-dihydroxyxanthone

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ABSTRACT

Arylated xanthones were prepared by site-selective Suzuki–Miyaura reactions of the bis(triflate) of 1,3-dihydroxyxanthone. The first attack occurs at the sterically less encumbered position 3. The site-selectivity is in contrast to the bis(triflate) of 1,3-dihydroxyanthraquinone.

1. Introduction

Xanthones are an important family of oxygenated heterocyclic compounds that occur in a variety of higher plant families, such as Gentianaceae,[1] Guttiferae,[2] and in a few families of fungi and lichens (Fig. 1).[3] Some xanthone-containing plants, for example, *Cratoxylum cochinchinense* (*Lour.*), have been used as traditional medicines to treat fever, coughing, diarrhea, itching, ulcers, and abdominal complaints.[4] Lesch and Braese described the xanthone moiety as a so-called 'privileged structure', since members of this structural class are able to interact with different types of drug targets.[5] The great interest in synthetic and naturally occurring xanthones is due to their pharmacological properties. They have been reported to act as antioxidant,[6] antiallergic,[7] antibacterial,[8] antifungal,[9] anti-inflammatory,[10] antimalarial,[11] HIV-1 inhibitory,[12] antidepressant,[13] antidiabetic,[14] and antitumor agents. For example, paeciloxanthone has been reported to exhibit antitumor activity and AChE inhibition.[3] 5,6-Dimethylxanthone-4-acetic acid (DMXAA) is a synthetic small molecule that shows activity as a vascular disrupting agent.[15]

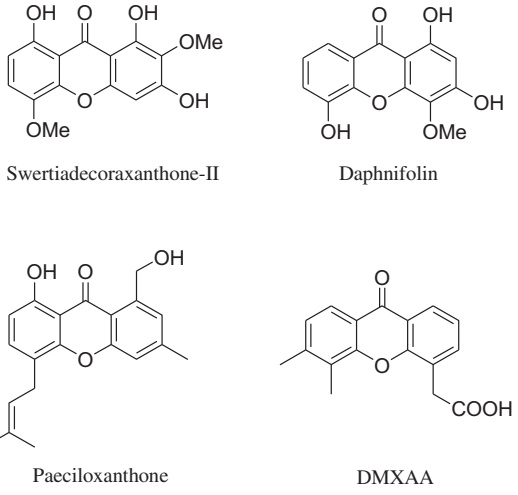

Fig. 1. Xanthone synthetic and natural products.

There are various known synthetic approaches to the xanthone framework. The classic ones involve the assembly of two benzene

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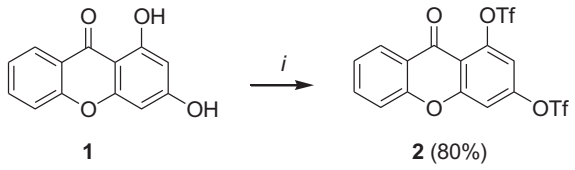
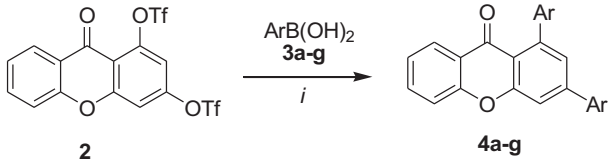
rings through a pyran unit.[16] The most commonly reported are the Friedel–Crafts acylation, Fries rearrangement and Ullmann condensation.[16] The direct formation of the xanthone moiety by reaction of arynes with substituted benzoates[17] or by Diels–Alder reaction[18] has also been reported. While the (known) biogenetic formation of xanthones largely dictates the nature and position of substituents,[19] the development of new synthetic approaches allows to prepare other types of substituted xanthones for biological screening. The presence of aryl groups located at the xanthone core has only been reported for a few synthetic derivatives. Arylated xanthones have been prepared by reaction of 3-(1-alkynyl)chromones with 1,3-dicarbonyl compounds[20] or acetonitriles[21] or by condensation of 2-methylchromone with cinnamaldehydes.[22] Arylated xanthones have also been synthesized by using transition metal catalyzed reactions, such as the domino Heck reaction of 3-bromo-2-styryl-chromones and styrenes[23–25] or by Suzuki cross-coupling reactions of brominated xanthones.[26] Herein, we report the synthesis of arylated xanthones by Suzuki–Miyaura reactions of the bis(triflate) of 1,3-dihydroxyxanthone. The reactions proceed with excellent site-selectivity in favor of position 3.

The reaction of 1,3-(dihydroxy)xanthone with triflic anhydride afforded the bis(triflate) **2** in 80% yield (Scheme 1).



Scheme 1. Synthesis of **2**. Conditions: i, **1** (1.0 equiv), Tf_2O (2.4 equiv), pyridine (4.0 equiv), CH_2Cl_2, 20 °C, 12 h.

The reaction of bis(triflate) **2** with arylboronic acids **3a**–**g** (2.4 equiv) afforded the 1,3-diarylxanthones **4a**–**g** in 70–95% yield (Scheme 2, Table 1). The best yields were obtained when the reaction was carried out using $Pd(PPh_3)_2Cl_2$ (10 mol %) as the catalyst, KF (6.6 equiv) as the base, and toluene as the solvent (Table 2). Both electron rich and electron poor arylboronic acids could be successfully employed.



Scheme 2. Synthesis of **4a**–**g**. Conditions: i, **2** (1.0 equiv), $ArB(OH)_2$ (2.4 equiv), $Pd(PPh_3)_2Cl_2$ (10 mol %), KF (6.6 equiv), toluene, 120 °C, 5 h.

Table 1
Synthesis of 1,3-diarylxanthones **4a**–**g**

3,4	Ar	% (**4**)[a]
a	4-(MeO)C_6H_4	95
b	2-(MeO)C_6H_4	75
c	4-EtC_6H_4	90
d	3,5-$Me_2C_6H_3$	70
e	3-ClC_6H_4	85
f	4-ClC_6H_4	81
g	4-FC_6H_4	73

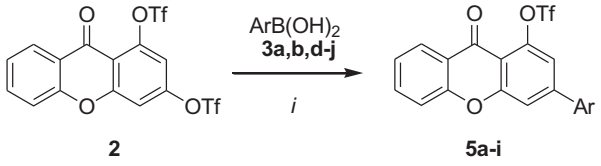
[a] Yields of isolated compounds.

Table 2
Optimization of the synthesis of **4a**,**g** (all reactions were carried out at 120 °C for 5 h)

Entry	Base[a]	Solvent[b]	Catalyts[c]	% (**4a**)[d]	% (**4g**)[d]
1	K_3PO_4	Dioxane	$[Pd(PPh_3)_4]$	42	25
2	K_3PO_4	Toluene	$[Pd(PPh_3)_4]$	51	38
3	KF	Dioxane	$[Pd(PPh_3)_4]$	57	42
4	KF	Toluene	$[Pd(PPh_3)_4]$	65	47
5	K_3PO_4	Dioxane	$[Pd(PPh_3)_2\ Cl_2]$	49	33
6	K_3PO_4	Toluene	$[Pd(PPh_3)_2\ Cl_2]$	60	40
7	KF	Dioxane	$[Pd(PPh_3)_2\ Cl_2]$	74	58
8	KF	Toluene	$[Pd(PPh_3)_2\ Cl_2]$	95	73

[a] K_3PO_4 (3.0 equiv) or KF (6.6 equiv) per 0.15 mmol of **2**.
[b] 2 ml per 0.15 mmol of **2**.
[c] 10 mol % per 0.15 mmol of **2**.
[d] Yield of isolated products.

The reaction of bis(triflate) **2** with arylboronic acids **3a**,**b**,**d**–**j** (1.1 equiv) afforded the 3-aryl-1-(trifluoromethylsulfonyloxy)xanthones **5a**–**i** in 72–91% yield (Scheme 3, Table 3). The best yields were obtained when the reaction was carried out using $Pd(PPh_3)_4$ (3 mol %) as the catalyst, K_3PO_4 (1.5 equiv) as the base, and dioxane as the solvent. Both electron rich and electron poor as well as functionalized arylboronic acids could be successfully employed. While the synthesis of **4a**–**g** was carried out at 120 °C, the synthesis of **5a**–**i** had to be carried out at 80 °C to achieve a good site-selectivity. Mixtures of mono- and diarylated products were obtained when the reaction was carried out at 120 °C. The structure of **5i** was independently confirmed by X-ray crystal structure analysis (Fig. 2).[27]



Scheme 3. Synthesis of **5a**–**i**. Conditions: i, **2** (1.0 equiv), $ArB(OH)_2$ (1.1 equiv), $Pd(PPh_3)_4$ (3 mol %), K_3PO_4 (1.5 equiv), dioxane, 80 °C, 7 h.

Table 3
Synthesis of **5a**–**i**

3	5	Ar	% (**5**)[a]
a	**a**	4-(MeO)C_6H_4	90
b	**b**	2-(MeO)C_6H_4	77
c	**c**	3,5-$Me_2C_6H_3$	72
d	**d**	3-ClC_6H_4	80
e	**e**	4-ClC_6H_4	85
f	**f**	4-FC_6H_4	76
g	**g**	4-*t*BuC_6H_4	91
h	**h**	4-(MeCO)C_6H_4	83
i	**i**	4-$CF_3C_6H_4$	86

[a] Yields of isolated compounds.

The one-pot reaction of bis(triflate) **2** with two different arylboronic acids (sequential addition) afforded the 1,3-diarylxanthones **6a**–**e** in 63–85% yield (Scheme 4, Table 4). The best yields were obtained when the reaction was carried out using, for the first step, $Pd(PPh_3)_2Cl_2$ (3 mol %), KF (3.3 equiv), and toluene (85 °C, 16 h) and, for the second step, an additional amount of $Pd(PPh_3)_2Cl_2$ (6 mol %) (120 °C, 7 h). Both in the first and second step of the one-pot reaction, electron poor and rich arylboronic acids could be successfully used.

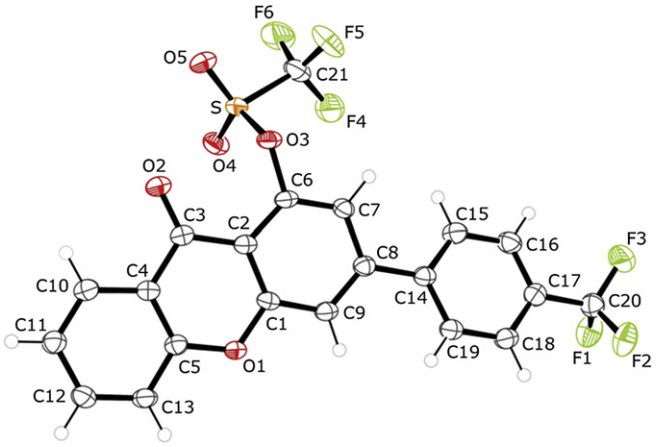
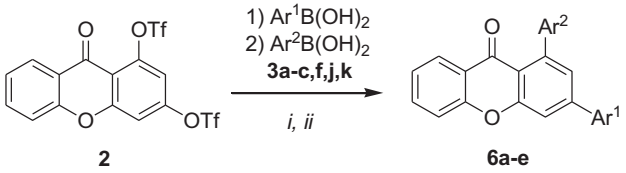


Fig. 2. Molecular structure of compound **5i**.



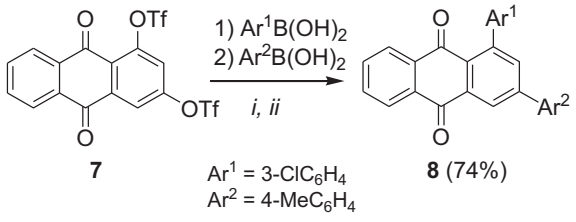
Scheme 4. Synthesis of **6a**–**e**. Conditions: i, **2** (1.0 equiv), $Ar^1B(OH)_2$ (1.0 equiv), $Pd(PPh_3)_2Cl_2$ (3 mol %), KF (3.3 equiv), toluene, 85 °C, 16 h. ii, $Ar^2B(OH)_2$ (1.4 equiv), $Pd(PPh_3)_2Cl_2$ (6 mol %), 120 °C, 7 h.

Table 4
Synthesis of **6a**–**e**

3	6	Ar^1	Ar^2	% (**6**)[a]
c,**f**	**a**	4-EtC_6H_4	4-ClC_6H_4	70
h,**a**	**b**	4-*t*BuC_6H_4	4-(MeO)C_6H_4	78
g,**b**	**c**	4-FC_6H_4	2-(MeO)C_6H_4	81
g,**k**	**d**	4-FC_6H_4	2-MeC_6H_4	63
j,**a**	**e**	4-$CF_3C_6H_4$	4-(MeO)C_6H_4	85

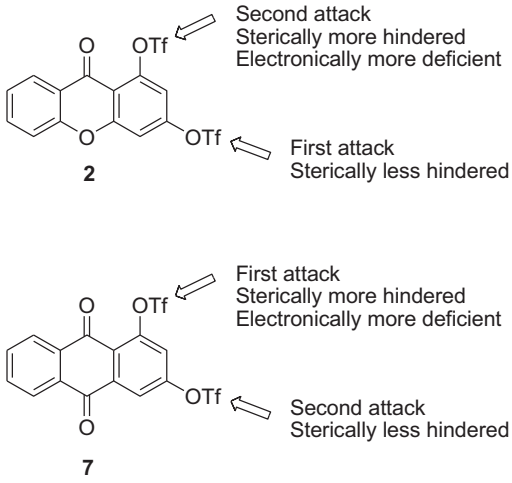
[a] Yields of isolated compounds.

We have earlier reported that the one-pot reaction of the bis(triflate) **7** of 1,3-dihydroxyanthraquinone with two different arylboronic acids afforded 1,3-diaryl-anthraquinones, such as derivative **8** (Scheme 5). The first attack occurred at position 1.[28]



Scheme 5. Synthesis of **8a**,**b**. Conditions: i, **4** (1.0 equiv), $Ar^1B(OH)_2$ (1.0 equiv), $Pd(PPh_3)_4$ (3 mol %), K_3PO_4 (3.0 equiv), dioxane, 60 °C, 30 h; ii, $Ar^2B(OH)_2$ (1.2 equiv), $Pd(PPh_3)_4$ (3 mol %), 100 °C, 5 h.

Palladium catalyzed cross-coupling reactions usually proceed by site-selective attack to the more electron deficient or less sterically hindered position.[29] In case of bis(triflate) **2**, the site-selectivity in favor of position 3 can be explained by the fact that position 3 is less sterically hindered than position 1 (Scheme 6). On the other hand, position 1 is more electron deficient. As mentioned above, we have earlier observed that Suzuki–Miyaura reactions of bis(triflate) **7** of 1,3-dihydroxyanthraquinone proceed with very good site-selectivity in favor of position 1 (Scheme 5).[28] The ^1H NMR chemical shifts of the parent compounds, in which the OTf or Br group is replaced by a hydrogen atom, have been reported to represent a good tool to predict the electronic character of the atoms and to predict the regioselectivity of palladium(0) catalyzed cross-coupling reactions.[30] The ^1H NMR chemical shifts (in $CDCl_3$) of anthraquinone are 8.34 ppm (1-H) and 7.80 ppm (3-H), while the values for xanthone are 8.32 ppm (1-H) and 7.70 ppm (3-H). The chemical shifts of the protons 1-H and 3-H of both respective compounds are very similar. Therefore, the change of the regioselectivity is surprising. It might be explained by the electron donating effect of the oxygen atom of the xanthone ring.



Scheme 6. Possible explanation for the site-selectivity of the Suzuki reactions of **2**.

2. Experimental section

2.1. Synthesis of 9-oxo-9*H*-xanthene-1,3-diyl bis(trifluoromethanesulfonate) (2)

To a CH_2Cl_2 (50 ml) solution of 1,3-dihydroxy-9*H*-xanthen-9-one **1** (1.0 g, 4.4 mmol) pyridine (1.42 ml, 17.6 mmol) and Tf_2O (1.8 ml, 10.6 mmol) were added and reaction mixture was stirred at 20 °C under argon atmosphere for 12 h. In the reaction mixture toluene (20 ml) was added and concentrated in vacuo. Residue was chromatographed (EtOAc/heptanes) without aqueous work up to yield **2** as a white solid (1.73 g, 80%), mp: 156 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.05 (d, 1H, J=2.3 Hz, ArH), 7.37–7.45 (m, 2H, ArH), 7.49 (d, 1H, J=2.4 Hz, ArH), 7.73 (ddd, 1H, J=1.7, 7.1, 8.6 Hz, ArH), 8.28 (dd, 1H, J=1.6, 8.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.1, −72.2. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=111.9, 112.1 (CH), 115.5 (C), 117.6 (CH), 118.6 (q, $J_{C,F}$=320.9 Hz, CF_3), 118.8 (q, $J_{C,F}$=320.6 Hz, CF_3), 121.8 (C), 125.5, 127.1, 136.1 (CH), 148.6, 151.5, 155.1, 157.5 (C), 173.9 (CO). IR (KBr): ν=3104 (w), 1663 (m), 1611 (s), 1592, 1570, 1471, 1460 (m), 1423 (s), 1353, 1334 (w), 1312 (m), 1280 (w), 1273, 1237 (m), 1202 (s), 1165, 1150 (m), 1135, 1109 (s), 1044, 1020 (m), 991 (s), 922 (w), 884 (s), 855 (w), 842, 810, 799, 768, 758 (m), 722 (w), 712 (m), 697, 684, 682 (w), 614, 592, 585, 570 (m), 545 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=492 ($[M]^+$, 80), 428 (30), 364 (7), 336 (13), 267 (100). HRMS (EI, 70 eV): calcd for $C_{15}H_6F_6O_8S_2$ $[M]^+$: 491.94028; found: 491.94039.

2.2. General procedure A for Suzuki–Miyaura cross-coupling reactions to synthesize 4a–g

A toluene solution of 9-oxo-9*H*-xanthene-1,3-diyl bis(trifluoromethanesulfonate) **2** (0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), arylboronic acid (2.4 equiv), and KF (6.6 equiv) was heated at 120 °C for 5 h under argon atmosphere. After cooling to 20 °C, H_2O was added and the reaction mixture was extracted with CH_2Cl_2 (3×25 ml) organic layers were dried (Na_2SO_4), filtered and concentrated in vacuo. The residue was purified by column chromatography (EtOAc/heptanes).

*2.2.1. 1,3-Bis(4-methoxyphenyl)-9H-xanthen-9-one (**4a**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 4-methoxyphenylboronic acid (55 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), compound **4a** was isolated as a yellow solid (58 mg, 95%), mp: 196–198 °C. Reaction temperature: 120 °C for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.78, 3.80 (s, 6H, 2OCH_3), 6.90–6.95 (m, 4H, ArH), 7.22–7.27 (m, 3H, ArH), 7.29 (d, 1H, *J*=1.9 Hz, ArH), 7.39 (br d, 1H, *J*=8.3 Hz, ArH), 7.56–7.59 (m, 4H, ArH), 8.12 (dd, 1H, *J*=1.6, 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=54.2, 54.4 (OCH_3), 112.1, 113.3, 113.5, 116.3 (CH), 116.6, 121.9 (C), 122.7, 124.9, 125.9, 127.5, 128.8 (CH), 130.1, 133.2 (C), 133.3 (CH), 143.4, 144.7, 154.5, 156.8, 157.9, 159.4 (C), 175.7 (CO). IR (KBr): *v*=3060, 3044, 2995, 2962, 2917, 2838 (w), 1665, 1598 (s), 1553 (w), 1514 (s), 1474 (w), 1460, 1447 (s), 1430, 1388, 1355 (m), 1325 (w), 1309, 1283 (m), 1244, 1235 (s), 1189, 1176, 1169, 1148, 1109, 1099 (w), 1020 (s), 962, 944, 931, 924, 878, 851 (w), 820, 813, 793, 733 (s), 716, 698, 638, 621, 610, 602, 591, 581, 554 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=408 ([M]$^+$, 39), 407 ([M–H]$^+$, 100), 365 (08), 321 (10), 263 (05). HRMS (EI, 70 eV): calcd for $C_{27}H_{19}O_4$ [M–H]$^+$: 407.12779; found: 407.12780.

*2.2.2. 1,3-Bis(2-methoxyphenyl)-9H-xanthen-9-one (**4b**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 2-methoxyphenylboronic acid (55 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), **4b** was isolated as a yellow solid (46 mg, 75%), mp: 158–160 °C. Reaction temperature: 120 °C for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.62, 3.78 (s, 6H, 2OCH_3), 6.89–6.99 (m, 4H, ArH), 7.16–7.20 (m, 2H, ArH), 7.27–7.32 (m, 3H, ArH), 7.37 (d, 2H, *J*=7.9 Hz, ArH), 7.54–7.60 (m, 1H, ArH), 7.66 (d, 1H, *J*=1.6 Hz, ArH), 8.10 (dd, 1H, *J*=1.4, 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=55.6, 55.7 (OCH_3), 110.3, 111.4, 117.4, 118.3 (CH), 118.8 (C), 120.4, 121.0 (CH), 122.0 (C), 123.5, 126.8, 128.5, 128.7, 129.4, 129.9, 130.9 (CH), 131.5 (C), 134.1 (CH), 139.6, 144.1, 155.6 (C), 156.6 (2C), 157.1 (C), 175.7 (CO). IR (KBr): *v*=3058, 3023, 2997, 2936, 2917, 2836 (w), 1659 (s), 1618 (m), 1605, 1595 (s), 1580, 1554 (w), 1495, 1467, 1461 (s), 1433, 1396, 1356 (m), 1312, 1295, 1270 (w), 1241, 1230 (s), 1181, 1170, 1160, 1147, 1132, 1117, 1097, 1065 (w), 1045 (m), 1020 (s), 947, 931 (m), 885 (w), 870, 840 (m), 810, 791, 772 (w), 752 (s), 728 (m), 697 (w), 674 (m), 647, 622, 599, 572, 553 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=408 ([M]$^+$, 01), 378 (26), 377 (100), 362 (11), 361 (41). HRMS (EI, 70 eV): calcd for $C_{27}H_{20}O_4$ [M]$^+$: 408.13561; found: 408.13574.

*2.2.3. 1,3-Bis(4-ethylphenyl)-9H-xanthen-9-one (**4c**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 4-ethylphenylboronic acid (54 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), **4c** was isolated as a white solid (55 mg, 90%), mp: 123 °C. Reaction temperature: 120 °C for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.18–128 (m, 6H, 2CH_3), 2.58–2.73 (m, 4H, 2CH_2), 7.20–7.25 (m, 7H, ArH), 7.35 (d, 1H, *J*=1.8 Hz, ArH), 7.40 (br d, 1H, *J*=8.1 Hz, ArH), 7.57 (d, 2H, *J*=8.3 Hz, ArH), 7.60–7.64 (m, 2H, ArH), 8.13 (dd, 1H, *J*=1.4, 7.9 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=15.3, 15.5 (CH_3), 28.6, 28.7 (CH_2), 115.0, 117.4 (CH), 117.9, 122.9 (C), 123.8, 126.2, 127.0, 127.2, 127.3, 128.5, 128.6, 134.4 (CH), 136.2, 139.3, 143.0, 144.7, 145.7, 146.1, 155.6, 157.8 (C), 176.8 (CO). IR (KBr): *v*=3055, 3026, 2960, 2867, 2850 (w), 1658 (s), 1614 (w), 1598 (s), 1594 (w), 1574, 1519 (m), 1504 (w), 1467 (s), 1427 (m), 1408 (w), 1386, 1355 (m), 1335 (w), 1308 (s), 1261, 1199, 1186, 1170, 1144, 1121, 1108, 1100, 1060, 1019, 946 (w), 945, 928 (m), 897, 879, 862, 853 (w), 818, 756 (s), 727, 699, 670, 624, 606, 591, 582, 553, 532 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=404 ([M]$^+$, 47), 403 ([M–H]$^+$, 100), 388 (12), 373 (08). HRMS (EI, 70 eV): calcd for $C_{29}H_{23}O_2$ [M–H]$^+$: 403.16926; found: 403.16953.

*2.2.4. 1,3-Bis(3,5-dimethylphenyl)-9H-xanthen-9-one (**4d**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 3,5-dimethylphenylboronic acid (54 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), **4d** was isolated as a white solid (42 mg, 70%), mp: 173–175 °C. Reaction temperature: 120 °C for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.31 (br s, 12H, 4CH_3), 6.92 (br s, 2H, ArH), 6.99 (br s, 2H, ArH), 7.20–7.25 (m, 3H, ArH), 7.31 (d, 1H, *J*=1.8 Hz, ArH), 7.39 (dd, 1H, *J*=0.7, 8.4 Hz, ArH), 7.57–7.63 (m, 2H, ArH), 8.12 (dd, 1H, *J*=1.6, 8.0 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=21.4, 21.5 (2CH_3), 115.1, 117.4 (CH), 118.0, 122.9 (C), 123.7, 125.3, 126.2, 126.3, 127.0, 128.9, 130.4, 134.3 (CH), 136.9, 138.6, 138.8, 142.0, 144.8, 146.3, 155.5, 157.5 (C), 176.6 (CO). IR (KBr): *v*=3030, 2996, 2914, 2852, 2727 (w), 1665 (s), 1615 (w), 1597, 1555 (s), 1512 (w), 1475 (m), 1462 (s), 1387, 1379, 1359, 1309 (m), 1290, 1265 (w), 1224 (m), 1167, 1151, 1141, 1131, 1106, 1082, 1034, 1018, 966, 946 (w), 841 (s), 808 (w), 792 (m), 758 (s), 731, 709, 702, 684 (w), 674, 656, 643 (m), 625, 608, 589, 554, 545 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)= 404 ([M]$^+$, 53), 403 ([M–H]$^+$, 100), 389 (22). HRMS (EI, 70 eV): calcd for $C_{29}H_{23}O_2$ [M–H]$^+$: 403.16926; found: 403.16942.

*2.2.5. 1,3-Bis(3-chlorophenyl)-9H-xanthen-9-one (**4e**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 3-chlorophenylboronic acid (56 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), **4e** was isolated as a white solid (53 mg, 85%), mp: 146–148 °C. Reaction temperature: 120 °C for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.17–7.20 (m, 1H, ArH), 7.24–7.36 (m, 7H, ArH), 7.38–7.43 (m, 1H, ArH), 7.49–7.52 (m, 1H, ArH), 7.61–7.66 (m, 3H, ArH), 8.11 (dd, 1H, *J*=1.3, 8.0 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=116.1, 117.5 (CH), 118.3, 122.7 (C), 124.1, 125.6, 125.9 (CH), 126.9 (2 CH), 127.4, 127.5, 128.5, 128.8, 129.0, 130.4 (CH), 133.6 (C), 134.8 (CH), 135.2, 140.4, 143.3, 143.4, 144.8, 155.5, 157.6, 176.4 (CO). IR (KBr): *v*=3054, 2954, 2920, 2850 (w), 1655 (s), 1616 (m), 1601, 1592, 1554 (s), 1515, 1494 (w), 1461 (s), 1414 (w), 1397, 1354 (m), 1338, 1303, 1289 (w), 1227 (m), 1189, 1176, 1169, 1137, 1131, 1081, 1074, 1057, 947 (w), 933 (m), 894, 872 (w), 857 (s), 830, 806 (w), 779, 752 (s), 728, 676, 668 (m), 650, 624, 585 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=419 ([M–H, ^{37}Cl, ^{37}Cl]$^+$, 25), 417 ([M–H, ^{35}Cl, ^{37}Cl]$^+$, 59), 415 ([M–H, ^{35}Cl, ^{35}Cl]$^+$, 100), 381 (05). HRMS (EI, 70 eV): calcd for $C_{25}H_{13}Cl_2O_2$ [M–H, ^{35}Cl, ^{35}Cl]$^+$: 415.02871; found: 415.02871; calcd for $C_{25}H_{13}Cl_2O_2$ [M–H, ^{35}Cl, ^{37}Cl]$^+$: 417.02576; found: 417.02706.

*2.2.6. 1,3-Bis(4-chlorophenyl)-9H-xanthen-9-one (**4f**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 4-chlorophenylboronic acid (56 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), **4f** was isolated as a white solid (51 mg, 81%), mp: 206–208 °C. Reaction temperature: 120 °C for 5 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.21–7.27 (m, 4H, ArH), 7.32–7.40 (m, 5H, ArH), 7.55 (d, 2H, *J*=8.5 Hz, ArH), 7.60–7.65 (m, 2H, ArH), 8.10 (dd, 1H, *J*=1.4, 7.9 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=115.7, 117.5 (CH), 118.1, 122.7 (C), 124.1, 125.8, 126.9, 127.9, 128.6, 129.4, 129.9 (CH), 133.4 (C), 134.7 (CH), 135.3, 137.0, 140.1, 143.6, 145.0, 155.5, 157.7 (C), 176.6 (CO). IR (KBr): *v*=3103, 3087, 3069, 3053, 3034, 2952, 2918, 2850 (w), 1661 (s), 1618 (w), 1601 (s), 1547 (w), 1496, 1466 (m), 1420 (w), 1378, 1356 (m), 1340 (s), 1312, 1303 (w), 1296 (m), 1292, 1269 (w), 1108 (m), 964, 956 (w), 945 (m), 929, 907, 892, 872, 855 (w), 821, 809 (s), 759 (w), 750, 732 (m), 719, 704, 641,

618, 600 (w), 559, 547 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=419 ([M–H, ^{37}Cl, $^{37}Cl]^+$, 18), 417 ([M–H, ^{35}Cl, $^{37}Cl]^+$, 73), 415 ([M–H, ^{35}Cl, $^{35}Cl]^+$, 100), 379 (06). HRMS (EI, 70 eV): calcd for $C_{25}H_{13}Cl_2O_2$ [M–H, ^{35}Cl, $^{35}Cl]^+$: 415.02871; found: 415.02852; calcd for $C_{25}H_{13}Cl_2O_2$ [M–H, ^{35}Cl, $^{37}Cl]$: 417.02576; found: 417.02613.

*2.2.7. 1,3-Bis(4-fluorophenyl)-9H-xanthen-9-one (**4g**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_2Cl_2$ (10 mg, 10 mol %), 4-fluorophenylboronic acid (50 mg, 0.36 mmol), KF (58 mg, 1 mmol), and toluene (2 ml), **4g** was isolated as a white solid (42 mg, 73%), mp: 173–175 °C. Reaction temperature: 120 °C for 5 h. ^1H NMR (300 MHz, $CDCl_3$): δ=7.02–7.15 (m, 4H, ArH), 7.24–7.31 (m, 4H, ArH), 7.41 (dd, 1H,=*J* 0.6, 8.4 Hz, ArH), 7.58–7.65 (m, 4H, ArH), 8.11 (dd, 1H, *J*=1.6, 8.0 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−115.3, −112.7. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=114.6 (d, $J_{F,C}$=21.5 Hz, CH), 115.6 (CH), 116.2 (d, $J_{F,C}$=21.5 Hz, CH), 117.5 (CH), 118.0, 122.0 (C), 124.0, 126.1, 126.9 (CH), 129.1 (d, $J_{F,C}$=8.3 Hz, CH), 130.1 (d, $J_{F,C}$=7.7 Hz, CH), 134.7 (CH), 134.8 (d, $J_{F,C}$=3.3 Hz, C), 137.6 (d, $J_{F,C}$=3.9 Hz, C), 143.8, 145.2, 155.5, 157.7 (C), 162.0 (d, $J_{F,C}$=245.8 Hz, CF), 163.4 (d, $J_{F,C}$=249.3 Hz, CF), 176.7 (CO). IR (KBr): *v*=3060, 2921, 2852 (w), 1658 (s), 1619 (w), 1602, 1594 (s), 1551 (w), 1513, 1506, 1465 (s), 1426 (m), 1404 (w), 1380, 1357 (m), 1338 (w), 1313 (m), 1303 (w), 1222 (s), 1173 (w), 1156, 1145 (m), 1118, 1103, 1065, 1020, 1013, 960 (w), 945, 926 (m), 894, 867, 851 (w), 825 (s), 811, 779 (w), 753 (s), 733, 719, 697, 676, 668, 644, 637, 618, 604, 586, 569 (w), 549 (m) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=384 ($[M]^+$, 46), 383 ($[M-H]^+$, 100), 367 (04), 325 (04). HRMS (EI, 70 eV): calcd for $C_{25}H_{13}F_2O_2$ $[M-H]^+$: 383.08781; found: 383.08785.

2.3. General procedure B for Suzuki–Miyaura cross-coupling reactions to synthesize 5a–i

A 1,4-dioxane solution of of 9-oxo-9*H*-xanthene-1,3-diyl bis(-trifluoromethanesulfonate) **2** (0.15 mmol), $Pd(PPh_3)_4$ (3 mol %), arylboronic acid (1.1 equiv), and K_3PO_4 (1.5 equiv) was heated at 80 °C for 7 h under argon atmosphere. After cooling to 20 °C, CH_2Cl_2 (30 ml) was added and filtered then the filtrate was concentrated in vacuo. The residue was purified by column chromatography (EtOAc/heptanes).

*2.3.1. 4-(3-(4-Methoxyphenyl)-9-oxo-9H-xanthen-1-yl)phenyl trifluoromethanesulfonate (**5a**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 4-methoxyphenylboronic acid (24 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5a** was isolated as a white solid (61 mg, 90%), mp: 191–193 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=3.79 (s, 3H, OCH_3), 6.95 (d, 2H, *J*=8.7 Hz, ArH), 7.26–7.39 (m, 3H, ArH), 7.50 (d, 2H, *J*=8.8 Hz, ArH), 7.59 (d, 1H, *J*=1.5 Hz, ArH), 7.62–7.67 (m, 1H, ArH), 8.27 (dd, 1H, *J*=1.4, 7.9 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=55.4 (OCH_3), 113.5 (C), 114.8, 115.5, 115.9, 117.5 (CH), 118.9 (q, $J_{C,F}$=320.3 Hz, CF_3), 122.1 (C), 124.6, 126.9, 128.4 (CH), 129.4 (C), 135.3 (CH), 147.3, 147.9, 155.3, 157.3, 161.1 (C), 174.7 (CO). IR (KBr): *v*=3072, 3012, 2971, 2941, 2912, 2842 (w), 1658, 1628, 1609 (s), 1545 (w), 1519 (s), 1473 (w), 1461, 1406, 1360 (m), 1335 (w), 1315, 1300 (m), 1282, 1270 (w), 1240, 1224 (m), 1204 (s), 1179, 1166, 1150 (w), 1137 (s), 1113, 1086, 1066 (w), 1031, 1012 (s), 966 (w), 939 (m), 877, 871, 851 (w), 833, 814, 806, 782, 767, 759 (m), 741, 724, 691, 680, 667, 642 (w), 610 (m), 595 (s), 574, 550, 542 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=450 ($[M]^+$, 100), 317 (23), 302 (13), 289 (34), 258 (16), 246 (12), HRMS (EI, 70 eV): calcd for $C_{21}H_{13}F_3O_6S_1$ $[M]^+$: 450.03794; found: 450.03830.

*2.3.2. 4-(3-(2-Methoxyphenyl)-9-oxo-9H-xanthen-1-yl)phenyl trifluoromethanesulfonate (**5b**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 2-methoxyphenylboronic acid (24 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5b** was isolated as a white solid (52 mg, 77%), mp: 145–147 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=3.79 (s, 3H, OCH_3), 6.89–7.04 (m, 2H, ArH), 7.29–7.40 (m, 5H, ArH), 7.57–7.68 (m, 2H, ArH), 8.29 (dd, 1H, *J*=1.4, 7.9 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.4. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=55.5 (OCH_3), 111.6 (CH), 113.8 (C), 117.6 (CH), 118.9 (q, $J_{C,F}$=320.8 Hz, CF_3), 119.1, 119.4, 121.3 (CH), 122.1 (C), 124.5 (CH), 126.6 (C), 126.9, 130.5, 131.0, 135.2 (CH), 145.6, 146.9, 155.4, 156.5, 156.9 (C), 175.0 (CO). IR (KBr): *v*=3067, 3005, 2950, 2918, 2842 (w), 1659, 1627, 1609 (s), 1581, 1547, 1504 (w), 1471, 1463 (m), 1441 (w), 1422, 1406 (s), 1357 (m), 1334 (w), 1315 (m), 1286, 1271 (w), 1247, 1240 (m), 1225 (w), 1203 (s), 1163 (w), 1140 (s), 1125, 1111 (m), 1064, 1052 (w), 1035 (m), 1015 (s), 958 (w), 890 (s), 870 (m), 852 (w), 814 (s), 800 (w), 784 (m), 757, 750 (s), 721, 701, 682, 661, 634, 626, 606 (w), 592, 575 (s), 544 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=450 ($[M]^+$, 100), 317 (20), 302 (11), 299 (12), 289 (35), 271 (10), 258 (11). HRMS (EI, 70 eV): calcd for $C_{21}H_{13}F_3O_6S_1$ $[M]^+$: 450.03794; found: 450.03826.

*2.3.3. 4-(3-(3,5-Dimethylphenyl)-9-oxo-9H-xanthen-1-yl)phenyl trifluoromethanesulfonate (**5c**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 3,5-dimethylphenylboronic acid (24 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5c** was isolated as a white solid (48 mg, 72%), mp: 210 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=2.35 (s, 6H, $2CH_3$), 7.06 (s, 1H, ArH), 7.17 (br s, 2H, ArH), 7.29–7.37 (m, 2H, ArH), 7.42 (dd, 1H, *J*=0.6, 8.4 Hz, ArH), 7.65–7.71 (m, 2H, ArH), 8.30 (dd, 1H, *J*=1.5, 8.0 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3.^{13}C NMR (75.5 MHz, $CDCl_3$): δ=21.4 ($2CH_3$), 114.0 (C), 116.5, 116.6, 117.6 (CH), 118.9 (q, $J_{C,F}$=320.7 Hz, CF_3), 122.2 (C), 124.7, 125.0, 127.0, 131.4, 135.3 (CH), 137.3, 139.1, 147.8, 148.2, 155.4, 157.9 (C), 174.7 (CO). IR (KBr): *v*=3097, 3067, 3012, 2953, 2920, 2851, 2732, 2664 (w), 1661, 1626, 1610 (s), 1548, 1492 (w), 1464 (m), 1427 (s), 1407 (w), 1395 (m), 1375 (w), 1359 (m), 1310 (w), 1214, 1204, 1187 (s), 1160 (w), 1137 (s), 1110 (m), 1081 (w), 1038, 1016 (m), 957 (w), 914 (m), 901 (w), 843, 834 (s), 798 (w), 716, 749 (s), 722, 689 (w), 666 (m), 656, 631, 609 (w), 594, 572 (s), 547 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=448 ($[M]^+$, 100), 384 (40), 356 (20), 316 (65), 300 (17), 287 (44), 281 (13), 272 (11), 259 (16). HRMS (EI, 70 eV): calcd for $C_{22}H_{15}F_3O_5S_1$ $[M]^+$: 448.05868; found: 448.05883.

*2.3.4. 4-(3-(3-Chlorophenyl)-9-oxo-9H-xanthen-1-yl)phenyl-trifluoromethanesulfonate (**5d**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 3-chlorophenylboronic acid (25 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5d** was isolated as a white solid (55 mg, 80%), mp: 172 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=7.24 (d, 1H, *J*=0.8 Hz, ArH), 7.28–7.34 (m, 1H, ArH), 7.36–7.44 (m, 4H, ArH), 7.50–7.51 (m, 1H, ArH), 7.61–7.69 (m, 2H, ArH), 8.25 (dd, 1H, *J*=1.6, 8.0 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=114.4 (C), 116.3, 116.7, 117.6 (CH), 118.9 (q, $J_{C,F}$=321.1 Hz, CF_3), 122.1 (C), 124.8, 125.4, 126.9, 127.3, 129.7, 130.7 (CH), 135.4 (C), 135.5 (CH), 139.0, 146.1, 147.9, 155.2, 157.3 (C), 175.0 (CO). IR (KBr): *v*=3077, 2923, 2851, 2789, 2667 (w), 1665, 1627, 1607 (s), 1572, 1549, 1513 (w), 1502, 1470, 1460 (m), 1407 (w), 1392, 1357 (m), 1335 (w), 1310 (m), 1283, 1245 (w), 1222, 1192 (s), 1166 (m), 1136 (s), 1112, 1105, 1082 (w), 1032, 1012 (s), 995, 960 (w), 947 (m), 902 (s), 881, 862 (w), 823 (s), 800 (w), 785, 759, 721 (m), 694 (w), 678, 662 (m), 637, 631, 606 (w), 590, 572 (s), 548 (w) cm^{-1}. GC–MS (EI, 70 eV): *m*/*z* (%)=456 ([M, $^{37}Cl]^+$, 41), 454 ([M, $^{35}Cl]^+$, 100), 392 (21), 390 (62), 364 (11), 362 (29), 295 (11), 293 (39), 286 (28), 267 (16), 265 (43), 258 (26). HRMS (ESI-TOF/MS): calcd for $C_{20}H_{11}ClF_3O_5S_1$ [M+H, $^{35}Cl]^+$: 454.99623; found: 454.99651, calcd for $C_{20}H_{11}ClF_3O_5S$ [M+H, $^{37}Cl]^+$: 456.99351; found: 456.99363.

*2.3.5. 4-(3-(4-Chlorophenyl)-9-oxo-9H-xanthen-1-yl)phenyl trifluoromethanesulfonate (**5e**).* Starting with **2** (74 mg, 0.15 mmol),

$Pd(PPh_3)_4$ (5 mg, 3 mol %), 4-chlorophenylboronic acid (25 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5e** was isolated as a white solid (58 mg, 85%), mp: 200–202 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=7.27 (d, 1H, J=0.8 Hz, ArH), 7.32–7.37 (m, 1H, ArH), 7.39–7.52 (m, 5H, ArH), 7.64–7.71 (m, 2H, ArH), 8.29 (dd, 1H, J=1.5, 7.9 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=114.3 (C), 116.4, 116.5, 117.6 (CH), 118.9 (q, $J_{C,F}$=320.8 Hz, CF_3), 122.1 (C), 124.5, 127.0, 128.5, 129.7, 135.5 (CH), 135.7, 136.2, 146.4, 148.0, 153.3, 157.4 (C), 175.0 (CO). IR (KBr): ν=3110, 3076, 3038 (w), 1666, 1628, 1608 (s), 1591, 1547, 1505 (w), 1461 (m), 1426 (s), 1391, 1357, 1312 (m), 1285, 1267 (w), 1246 (m), 1221, 1194 (s), 1165 (w), 1091, 1031, 1010 (m), 965 (w), 937 (m), 887 (s), 866 (w), 830, 813, 798 (m), 760 (s), 723 (m), 689, 678 (w), 664 (m), 635, 620 (w), 607 (m), 590, 573 (s), 532 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=456 ([M, $^{37}Cl]^+$, 46), 454 ([M, $^{35}Cl]^+$, 100), 392 (18), 390 (61), 364 (09), 362 (30), 322 (20), 295 (13), 293 (35), 286 (23), 267 (12), 265 (33), 258 (38). HRMS (EI, 70 eV): calcd for $C_{20}H_{10}ClF_3O_5S_1$ [M, $^{35}Cl]^+$: 453.98841; found: 453.98857, calcd for $C_{20}H_{10}ClF_3O_5S_1$ [M, $^{37}Cl]^+$: 455.98546; found: 455.98437.

*2.3.6. 4-(3-(4-Fluorophenyl)-9-oxo-9H-xanthen-1-yl)phenyl trifluoromethanesulfonate (**5f**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 4-flourophenylboronic acid (23 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5f** was isolated as a white solid (50 mg, 76%), mp: 187 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=7.14 (t, 2H, J=8.6 Hz, ArH), 7.26 (d, 1H, J=0.8 Hz, ArH), 7.31–7.36 (m, 1H, ArH), 7.40 (br d, 1H, J=8.4 Hz, ArH), 7.52–7.58 (m, 2H, ArH), 7.62 (d, 1H, J=1.7 Hz, ArH), 7.67 (ddd, 1H, J=1.7, 7.0, 8.5 Hz, ArH), 8.28 (dd, 1H, J=1.6, 7.9 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−111.1, −73.3. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=114.4 (C), 116.4 (2CH), 116.6 (d, $J_{F,C}$=21.7 Hz, CH), 117.6 (CH), 118.9 (q, $J_{C,F}$=321.2 Hz, CF_3), 122.1 (C), 124.8, 127.0 (CH), 129.1 (d, $J_{F,C}$=8.6 Hz, CH), 133.5 (d, $J_{F,C}$=3.4 Hz, C), 135.5 (CH), 145.6, 148.0, 155.3, 157.3 (C), 163.8 (d, $J_{F,C}$=250.9 Hz, CF), 175.0 (CO). IR (KBr): ν=2922, 2852 (w), 1661, 1626, 1608 (s), 1550 (w), 1512, 1463 (m), 1435 (w), 1423 (s), 1404 (w), 1394, 1361 (m), 1334 (w), 1309 (m), 1286 (w), 1241, 1226 (m), 1216, 1197 (s), 1161, 1151 (w), 1134 (s), 1112, 1061 (w), 1037 (s), 938 (m), 872 (w), 823 (s), 819 (w), 797 (m), 770 (s), 760, 725, 700, 666, 659, 638 (w), 611, 594 (s), 571, 543 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=438 ([M]$^+$, 100), 374 (52), 346 (29), 305 (20), 277 (56), 249 (43), 220 (38). HRMS (EI, 70 eV): calcd for $C_{20}H_{10}F_4O_5S_1$ [M]$^+$: 438.01796; found: 438.01796.

*2.3.7. 4-(3-(4-(tert-Butyl)phenyl)-9-oxo-9H-xanthen-1-yl)phenyl-trifluoromethanesulfonate (**5g**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 4-*tert*-butylphenylboronic acid (29 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5g** was isolated as a white solid (64 mg, 91%), mp: 150–152 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=1.31 (s, 9H, $3CH_3$), 7.29–7.35 (m, 2H, ArH), 7.39 (br d, 1H, J=8.4 Hz, ArH), 7.46–7.54 (m, 4H, ArH), 7.64–7.70 (m, 2H, ArH), 8.28 (dd, 1H, J=1.5, 7.9 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=31.2 ($3CH_3$), 34.1, 113.7 (C), 116.1, 116.4, 117.6 (CH), 118.9 (q, $J_{C,F}$=320.2 Hz, CF_3), 122.1 (C), 124.7, 126.4, 126.9, 127.0 (CH), 134.3 (C), 135.3 (CH), 147.7, 147.9, 153.2, 155.3, 157.3 (C), 174.8 (CO). IR (KBr): ν=3075, 3040, 2965, 2924, 2868 (w), 1658, 1624, 1607 (s), 1545, 1524, 1494 (w), 1462, 1422 (s), 1397, 1359 (m), 1334, 1309, 1285, 1268, 1242, 1230 (w), 1209, 1186 (s), 1166 (m), 1137 (s), 1111 (m), 1080 (w), 1035, 1014 (s), 967 (w), 939, 895 (m), 881, 868, 853, 841 (w), 827, 813, 802, 770 (s), 724, 727, 721, 692 (w), 664 (m), 641, 622, 608 (w), 594 (s), 569, 545 (m) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=476 ([M]$^+$, 32), 461 (100), 328 (04), 300 (18), 254 (04). HRMS (ESI-TOF/MS): calcd for $C_{24}H_{20}F_3O_5S_1$ [M+H]$^+$: 477.09781; found: 477.09730.

*2.3.8. 4-(3-(4-Acetylphenyl)-9-oxo-9H-xanthen-1-yl)phenyl trifluoromethanesulfonate (**5h**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol %), 4-acetylphenylboronic acid (27 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5h** was isolated as a white solid (58 mg, 83%), mp: 203 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=2.58 (s, 3H, $COCH_3$), 7.31–7.40 (m, 3H, ArH), 7.63–7.69 (m, 4H, ArH), 8.0 (d, 2H, J=8.2 Hz, ArH), 8.3 (d, 1H, J=7.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=26.7 (CH_3), 114.6 (C), 116.5, 117.0, 117.6 (CH), 118.9 (q, $J_{C,F}$=321.1 Hz, CF_3), 122.1 (C), 124.9, 127.0, 127.5, 129.3, 135.6 (CH), 137.7, 141.4, 146.2, 148.0, 155.2, 157.3 (C), 174.7, 197.2 (CO). IR (KBr): ν=3105, 3076, 3005, 2919, 2850 (w), 1668, 1659, 1628, 1606 (s), 1545, 1519 (w), 1478, 1470 (m), 1422 (s), 1394, 1358 (m), 1337 (w), 1314 (m), 1287 (w), 1267, 1261, 1243 (m), 1208, 1199 (s), 1166, 1155 (w), 1134 (s), 1112, 1075, 1058 (w), 1034, 1012 (s), 961 (w), 938 (m), 887 (s), 863 (w), 834, 816, 802, 758 (s), 742, 720 (w), 665 (m), 623 (w), 609 (m), 595, 586, 573 (s), 550 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=462 ([M]$^+$, 76), 447 (96), 383 (31), 355 (26), 341 (11), 287 (21), 258 (28), 254 (14), 44 (100). HRMS (EI, 70 eV): calcd for $C_{22}H_{13}F_3O_6S_1$ [M]$^+$: 462.03794; found: 462.03783.

*2.3.9. 4-(9-Oxo-3-(4-(trifluoromethyl)phenyl)-9H-xanthen-1-yl) phenyl trifluoromethanesulfonate (**5i**).* Starting with **2** (74 mg, 0.15 mmol), $Pd(PPh_3)_4$ (5 mg, 3 mol -%), 4-(triflouromethyl)phenylboronic acid (31 mg, 0.17 mmol), K_3PO_4 (48 mg, 0.23 mmol), and dioxane (2 ml), **5h** was isolated as a white solid (63 mg, 86%), mp: 185–187 °C. Reaction temperature: 80 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=7.30–7.42 (m, 3H, ArH), 7.66–7.74 (m, 6H, ArH), 8.28 (dd, 1H, J=1.4, 7.9 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=−73.3, −62.8. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=114.7 (C), 116.6, 117.1, 117.6 (CH), 118.8 (q, $J_{C,F}$=320.9 Hz, CF_3), 122.1 (C), 123.8 (q, $J_{C,F}$=272.4 Hz, CF_3), 124.9 (CH), 126.4 (q, $J_{C,F}$=3.7 Hz, CH), 127.0, 127.7 (CH), 131.6 (q, $J_{C,F}$=32.3 Hz, C–CF_3), 135.6 (CH), 140.8, 146.1, 148.1, 155.3, 157.3 (C), 174.6 (CO). IR (KBr): ν=1660 (s), 1631, 1610 (m), 1548, 1524, 1474, 1463 (w), 1424 (s), 1399, 1360 (w), 1322, 1313 (s), 1243 (w), 1219, 1210 (s), 1177, 1156 (w), 1137, 1125, 1110, 1072 (s), 937, 899 (w), 889 (m), 877 (w), 844 (s), 814, 802 (m), 766, 761 (s), 736, 725, 703, 683, 672, 655, 624 (w), 596 (s), 550, 534 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=488 ([M]$^+$, 100), 469 (10), 424 (83), 396 (37), 355 (12), 327 (42), 299 (66), 258 (18). HRMS (EI, 70 eV): calcd for $C_{21}H_{10}F_6O_5S_1$ [M]$^+$: 488.01476; found: 488.01455.

2.4. General procedure C for the one-pot synthesis of 1,3-diarylxanthones 6a–e

A toluene solution9-oxo-9*H*-xanthene-1,3-diyl bis(trifluoromethanesulfonate) **2** (0.2 mmol), $Pd(PPh_3)_2Cl_2$ (3 mol %), $Ar^1B(OH)_2$ (1.0 equiv), and KF (3.3 equiv) was heated at 85 °C for 16 h under argon atmosphere. After cooling to 20 °C, $Ar^2B(OH)_2$ (1.4 equiv), $Pd(PPh_3)_2Cl_2$ (6 mol %), and KF (3.3 equiv), were added reaction mixture was heated at 120 °C for further 7 h. Reaction mixture was cooled again to 20 °C, H_2O was added and the reaction mixture was extracted with CH_2Cl_2 (3×25 ml), organic layers were dried (Na_2SO_4), filtered and then concentrated in vacuo. The residue was purified by column chromatography (EtOAc/heptanes).

*2.4.1. 1-(4-Chlorophenyl)-3-(4-ethylphenyl)-9H-xanthen-9-one (**6a**).* Starting with **2** (100 mg, 0.20 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 3 mol %) 4-ethylphenylboronic acid (30 mg, 0.20 mmol), KF (38 mg, 0.66 mmol), toluene (3 ml), and $Pd(PPh_3)_2Cl_2$ (8 mg, 6 mol %), 4-chlorophenylboronic acid (44 mg, 0.28 mmol), KF (38 mg, 0.66 mmol), **6a** was prepared according to the general procedure C, as a white solid (57 mg, 70%), mp: 195–197 °C. Reaction temperature was 85 °C for 16 h and 120 °C for 7 h. ^1H NMR (300 MHz, $CDCl_3$): δ=1.20 (t, 3H, J=7.7 Hz, CH_3), 2.63 (q, 2H, J=7.6 Hz, CH_2), 7.20–7.25 (m, 5H, ArH), 7.28 (d, 1H, J=1.8 Hz, ArH), 7.32 (d, 2H, J=8.4 Hz, ArH), 7.38 (br d, 1H, J=8.3 Hz, ArH), 7.54 (d, 2H, J=8.2 Hz,

ArH), 7.58–7.65 (m, 2H, ArH), 8.10 (dd, 1H, J=1.5, 7.9 Hz, ArH). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=14.4 (CH_3), 27.8 (CH_2), 114.4, 116.4 (CH), 116.7, 121.7 (C), 122.9, 124.8, 125.8, 126.2, 126.6, 127.3, 128.9 (CH), 132.2 (C), 133.5 (CH), 134.8, 139.3, 142.2, 144.4, 145.3, 154.5, 156.6 (C), 175.6 (CO). IR (KBr): ν=3063, 3031, 2960, 2927, 2869, 1956, 1925, 1866 (w), 1660 (s), 1614 (m), 1600 (s), 1574, 1553, 1519, 1488 (w), 1467, 1460 (m), 1426 (w), 1386, 1355, 1311 (m), 1295, 1262 (w), 1230 (m), 1194, 1172, 1146, 1124, 1100 (w), 1014 (m), 996, 965 (w), 944, 929 (m), 874, 861, 852, 835 (w), 825, 816, 764 (s), 730, 705, 697 (w), 671 (m), 640, 623, 603, 590 (w), 552 (m) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=412 ([M, ^{37}Cl]$^+$, 18), 410 ([M, ^{35}Cl]$^+$, 53), 409 ([M–H, ^{35}Cl]$^+$, 100), 394 (20), 373 (08). HRMS (ESI-TOF/MS): calcd for $C_{27}H_{20}ClO_2$ [M+H, ^{35}Cl]$^+$: 411.11463; found 411.11476, calcd For $C_{27}H_{20}ClO_2$ [M+H, ^{37}Cl]$^+$: 413.11288; found 413.11290.

*2.4.2. 3-(4-(tert-Butyl)phenyl)-1-(4-methoxyphenyl)-9H-xanthen-9-one (**6b**).* Starting with **2** (100 mg, 0.20 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 3 mol %) 4-*tert*-butylphenylboronic acid (36 mg, 0.20 mmol), KF (38 mg, 0.66 mmol), toluene (3 ml), and $Pd(PPh_3)_2Cl_2$ (8 mg, 6 mol %), 4-methoxyphenylboronic acid (43 mg, 0.28 mmol), KF (38 mg, 0.66 mmol), **6b** was prepared according to the general procedure C, as a white solid (68 mg, 78%), mp: 225–227 °C. Reaction temperature was 85 °C for 16 h and 120 °C for 7 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.30 (s, 9H, $3CH_3$), 3.79 (s, 3H, OCH_3), 6.91 (d, 2H, J=8.8 Hz, ArH), 7.21–7.27 (m, 3H, ArH), 7.33 (d, 1H, J=1.8 Hz, ArH), 7.36–7.44 (m, 3H, ArH), 7.55–7.59 (m, 3H, ArH), 7.61 (d, 1H, J=1.8 Hz, ArH), 8.12 (dd, 1H, J=1.5, 7.9 Hz, ArH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ=31.3 ($3CH_3$), 34.7 (C), 55.2 (OCH_3), 113.1, 114.9, 117.3 (CH), 117.9, 122.9 (C), 123.8, 126.1, 126.3, 126.9, 127.1, 129.8 (CH), 134.2 (C), 134.3 (CH), 135.9, 144.4, 145.9, 152.1, 155.1, 157.5, 158.9 (C), 176.8 (CO). IR (KBr): ν=3034, 2953, 2910, 2866, 2838 (w), 1650 (s), 1612 (m), 1599 (s), 1549 (w), 1467 (s), 1422, 1386 (w), 1311, 1282 (m), 1245 (s), 1173 (m), 1151, 1124, 1104 (w), 1024, 948, 927 (m), 915, 882, 868, 854, 848 (w), 821, 769 (s), 761, 723 (m), 689 (w), 676 (m), 646, 624, 606, 581, 557, 546, 528 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=434 ([M]$^+$, 85), 433 ([M–H]$^+$, 100), 419 (17), 417 (08), 390 (07). HRMS (EI, 70 eV): calcd for $C_{30}H_{25}O_3$ [M–H]$^+$: 433.17982; found: 433.17978; calcd for $C_{30}H_{26}O_3$ [M]$^+$: 434.18765; found: 434.18620.

*2.4.3. 1-(4-Methoxyphenyl)-3-(4-(trifluoromethyl)phenyl)-9H-xanthen-9-one (**6e**).* Starting with **2** (100 mg, 0.20 mmol), $Pd(PPh_3)_2Cl_2$ (4 mg, 3 mol %) 4-(trifluoromethyl)phenylboronic acid (38 mg, 0.20 mmol), KF (38 mg, 0.66 mmol), toluene (3 ml), and $Pd(PPh_3)_2Cl_2$ (8 mg, 6 mol %), 4-methoxylphenylboronic acid (43 mg, 0.28 mmol), KF (38 mg, 0.66 mmol), **6d** was prepared according to the general procedure C, as a yellow solid (76 mg, 85%), mp: 195–197 °C. Reaction temperature was 85 °C for 16 h and 120 °C for 7 h. ^{1}H NMR (300 MHz, $CDCl_3$): δ=3.81 (s, 3H, OCH_3), 6.91 (d, 2H, J=8.6 Hz, ArH), 7.23–7.28 (m, 3H, ArH), 7.33 (d, 1H, J=1.9 Hz, ArH), 7.41 (br d, 1H, J=8.1 Hz, ArH), 7.60–7.75 (m, 6H, ArH), 8.13 (dd, 1H, J=1.5, 8.1 Hz, ArH). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ=–62.6. ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=54.2 (OCH_3), 112.2, 114.6, 116.4 (CH), 117.7, 121.8 (C), 122.9 (CH), 123.0 (q, $J_{C,F}$=272.4 Hz, CF_3), 125.1 (q, $J_{C,F}$=3.9 Hz, CH), 125.3, 125.9, 126.7, 128.7 (CH), 129.7 (q, $J_{C,F}$=32.5 Hz, C–CF_3), 132.7 (C), 133.6 (CH), 141.4, 143.4, 143.9, 154.4, 156.7, 158.0 (C), 175.7 (CO). IR (KBr): ν=3078, 3052, 3031, 2966, 2920, 2828, 2087, 1946, 1923 (w), 1652 (s), 1613 (m), 1599 (s), 1575, 1548 (m), 1513, 1468 (s), 1454, 1446 (m), 1321, 1309 (s), 1292 (m), 1261, 1251 (s), 1230, 1206, 1176 (w), 1160 (m), 1146 (w), 1107, 1070, 1026, 1013 (s), 970, 956, 926, 888, 853 (w), 836, 830 (s), 801 (m), 758 (s), 736, 728, 704, 681, 670, 565, 624, 611, 601, 589, 578, 556, 530 (w) cm^{-1}. GC–MS (EI, 70 eV): m/z (%)=446 ([M]$^+$, 58), 445 ([M–H]$^+$, 100), 402 (20). HRMS (EI, 70 eV): calcd for $C_{27}H_{16}F_3O_3$ [M–H]$^+$: 445.10461; found: 445.10501, calcd for. $C_{27}H_{17}F_3O_3$ [M]$^+$: 446.11243; found: 446.11099.

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