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Cu(0)/Selectfluor system-catalyzed intramolecular C_{sp2}-H/C_{sp2}-H cross-dehydrogenative coupling (CDC)

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ABSTRACT

A Cu(0)/Selectfluor system-catalyzed intramolecular C_{sp2}-H/C_{sp2}-H bond cross-dehydrogenative coupling of 2-aryloxybenzaldehydes is described. A variety of substituted xanthone derivatives are synthesized in moderate to excellent yields. Reaction can also be extended to the synthesis of 9*H*-thioxanthen-9-one 10,10-dioxide and phenanthridin-6(5*H*)-ones, respectively.

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1. Introduction

The cross-coupling reaction is among the most efficient and powerful approaches for the formation of C—C and C-X (X = heteroatoms) bonds, which is the essential step for the construction of complex molecules [1–4]. During the past several decades, many studies on the cross-coupling reactions have been documented [1–4]. As for the formation of C—C bond is concerned, generally three types of cross-coupling mode have been developed: 1) the cross coupling between an organometallic reagent and an organohalide (or pseudohalide) (Scheme 1a) [1], 2) the cross coupling between an organometallic reagent (or organohalide) and an inert C—H bond (Scheme 1b) [3], and 3) the cross coupling between two inert C—H bonds (Scheme 1c) [4]. The third mode of cross-coupling was named by Li as "cross-dehydrogenative coupling (CDC)" [4a], which apparently has advantages of no requirement for the pre-functionalized coupling partners, step- and atom-economy, and environmental benignity. As such, in recent years, the application of CDC strategy in the construction of complex molecules has received much attention in organic synthesis [4,5].

Xanthone derivatives are a class of important heterocycles exhibiting a wide variety of biological and pharmacological activities such as anticancer, antioxidant, and antibacterial, etc. [6] Therefore, much effort has been taken to develop efficient methods for their preparation [5,7]. Beyond several traditional methods including the Friedel-Crafts cyclization of 2-aryloxybenzoyl(pseudo)halide [7b-f], acid-promoted dehydration of 2-aryloxybenzoic acids [7g,h], and dehydrofluorination of 2-hydroxyl-2′-flurobenzophenones [7i], in recent years, the application of CDC strategy for the construction of xanthone scaffold has received increasingly attention due to its many advantages mentioned above [5]. Despite some progress being made, there are still some limitations associated with the preparation of xanthones using CDC strategy. These include the use of expensive and toxic transition metal catalysts, the use of potentially explosive oxidants, harsh reaction conditions (usually > 120 °C), and/or low yields. Therefore, it is still highly desirable to develop novel CDC-related methods for the preparation of xanthones by using more economical and environmentally benign catalysts under relatively mild reaction conditions.

As part of our continued interest in the development of novel copper-catalyzed reactions [8], we currently focused on the Cu(0)/Selectfluor system-catalyzed highly efficient transformations [8a-g]. In our previous work, we disclosed that the combination of copper powder and Selectfluor (1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo-[2.2.2]octane bis(tetrafluoroborate), F-TEDA-BF_4)

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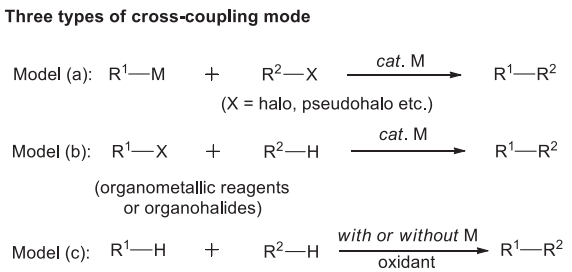


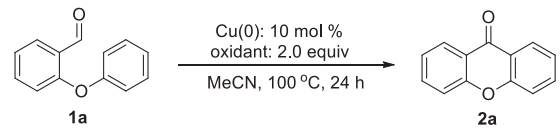
Scheme 1. Three types of cross-coupling mode for the formation of C–C bonds.

enabled in situ generation of an active copper(II) species HOCuX (X = F or BF_4), which has been proven to exhibit versatile reactivity in the Cu(0)/Selectfluor system-catalyzed tandem reactions (Scheme 2) [8a-g]. For example, this active HOCuX (X = F or BF_4) could readily undergo oxycupration toward carbon-carbon multiple bonds and induce successive tandem reactions (Scheme 2a-d) [8a-e]. It could activate allyl sp^3C–H bonds and induce successive oxidation reactions (Scheme 2e) [8f]. Recently, we found that this active HOCuX (X = F or BF_4) could even undergo oxycupration toward C=O bonds and trigger successive C–H bond functionalizations (Scheme 2f) [8g]. In view of the strong basicity of the OH^- anion in HOCuX species and the high efficiency of Cu(II) in C–H bond functionalizations [9], we envisioned that the in situ generated HOCuX might be able to abstract a proton from the formyl group in 2-aryloxybenzaldehydes and thus guide successive intramolecular cross-dehydrogenative coupling to deliver xanthone derivatives (Scheme 2g). Herein we would like to describe our concept for the synthesis of xanthone derivatives involving the Cu(0)/Selectfluor system-catalyzed cross-dehydrogenative coupling of 2-aryloxybenzaldehydes.

2. Results and discussion

Initially, we selected 2-phenoxybenzaldehyde **1a** as the model substrate for the optimization of the reaction conditions (Table 1). When **1a** was treated with 10 mol % of Cu(0) powder and 2 equivalents of Selectfluor in newly purchased MeCN (water content: 0.05 w/w %) at room temperature for 24 h, **2a** was not detected and the starting material was recovered (entry 1, Table 1).

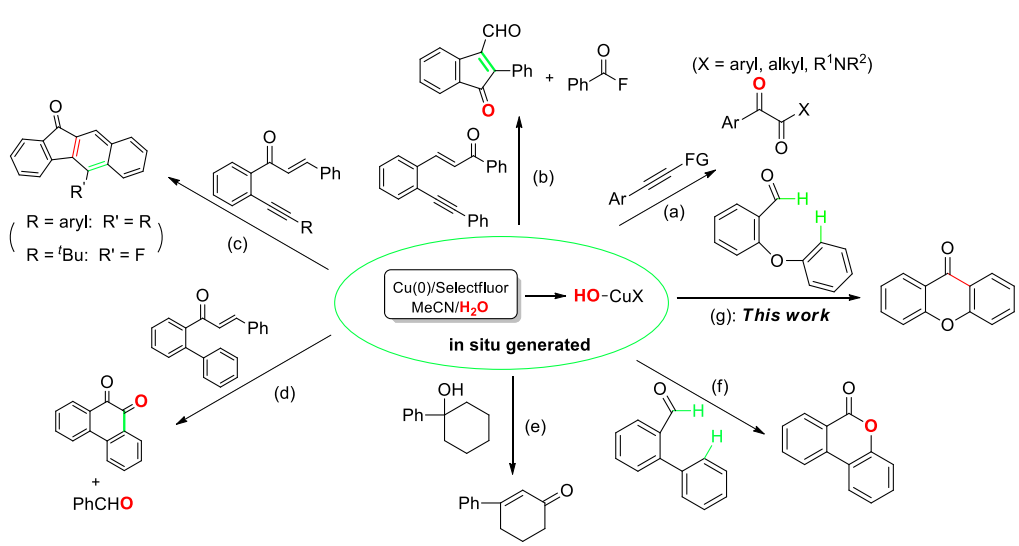
Table 1
Optimization of reaction conditions[a].



entry	catalyst	oxidant	solvent	yield (%)[b]
1	Cu(0)	Selectfluor	MeCN	0[c]
2	Cu(0)	Selectfluor	MeCN	54[c]
3	Cu(0)	Selectfluor	MeCN	72[c]
4	**Cu(0)**	**Selectfluor**	**MeCN**	**93(89[d])**
5	Cu(0)	NFSI[e]	MeCN	87
6	Cu(0)	$PhI(OOCCF_3)_2$	MeCN	22
7	Cu(0)	TBHP[f]	MeCN	15
8	Cu(0)	$K_2S_2O_8$	MeCN	0
9	Cu(0)	Selectfluor	DMF	50
10	Cu(0)	Selectfluor	DMSO	10
11	Cu(0)	Selectfluor	DCE	0
12	Cu(0)	Selectfluor	toluene	trace
13	Cu(0)	–	MeCN	0
14	–	Selectfluor	MeCN	53
15	Cu(0)	Selectfluor	MeCN	65[g],85[g]

[a] Reaction conditions: **1a** (0.3 mmol), catalyst (10 mol %), oxidant (2.0 equiv based on **1a**), MeCN (water content: 0.05 w/w %, 3 mL) at 100 °C unless otherwise noted.
[b] GC yield.
[c] At room temperature, 50 °C, and 80 °C for 24 h, respectively.
[d] Isolated yield.
[e] NFSI = N-Fluorobenzenesulfonimide.
[f] TBHP: *tert*-butyl hydroperoxide.
[g] 1.0 and 3.0 equiv of Selectfluor was used, respectively.

The yield of **2a** was gradually increased upon raising the reaction temperatures and it was found that 100 °C was a suitable temperature for getting satisfactory yield of **2a** (up to 93% yield, entries 2–4, Table 1). Besides Selectfluor, other electrophilic fluorinating reagent such as NFSI (N-fluorobenzenesulfonimide) could also afford good yield (87%, entry 5, Table 1). However, when $PhI(OOCCF_3)_2$, TBHP, or $K_2S_2O_8$ was respectively used as the oxidant, the reaction delivered **2a** in much lower yield compared to the case that Selectfluor was used as the oxidant (entries 6–8 vs 4, Table 1). In addition, solvent screening experiments were carried out and acetonitrile was proven to be the most suitable solvent for



Scheme 2. The Cu(0)/Selectfluor system-catalyzed tandem reactions.

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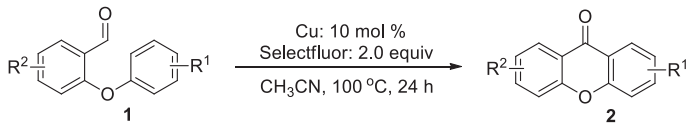
the reaction (entries 9–12 vs 4, Table 1). Control experiments indicated that Selectfluor was indispensable for the reaction, and 2.0 equivalents of Selectfluor were just enough for getting satisfactory yield of **2a** (entries 13, 15 vs 4, Table). It is surprised that the reaction could still proceed in the absence of the copper powder, albeit providing lower yields of **2a** (53%, entry 14, Table 1).

With the optimized reaction conditions in hand (Table 1, entry 4), we then set out to investigate the scope of 2-aryloxybenzaldehydes **1** and the results were shown in Table 2. First, the effect of substituents on the phenoxy ring (R^1) on the reaction was investigated. It was found that R^1 could either be electron-donating or electron-withdrawing groups. Generally speaking, there is no obvious regularity in terms of yields between substrates containing electron-rich phenoxy rings and those with electron-deficient phenoxy rings (**1a**-**1h**, Table 2). If substituents R^1 are at the 3-position of the phenoxy parts, the reaction would afford regioisomers. For example, when substrate **1i** was used, regioisomers **2i** and **2i′** were isolated in 45% and 30% yield, respectively; in case of **1j** as the substrate, the reaction afforded regioisomers **2j** and **2j′** in 55% and 33% yield, respectively. In addition, the effect of substituents R^2 on the reaction was also evaluated. It was found that **1** possessing either electron-donating or electron-withdrawing functional groups R^2 could undergo the present CDC reaction smoothly and deliver the corresponding products in moderate to excellent yields (49–95%, **2l**-**2w**, Table 2). Note that the R^2 substituents could be located at the *ortho*-, *meta*-as well as the *para*-position to the formyl group in **1**, and in most cases the reaction could perform well except in the case of **1n** affording the desired product in lower yield (49%, **2n**, Table 2). Finally, a gram-scale (5 mmol of **1a** used) synthesis of **2a** was also carried out, and the desired xanthone **1a** was obtained in 80% yield (in Supporting Information).

The exploration of the Cu(0)/Selectfluor system for other CDC reactions were further carried out (Scheme 3). First, when 2-(4-fluorophenylthio)benzaldehyde **3** was subjected to the optimal reaction conditions, the reaction, however, afforded 2-(4-fluorophenylsulfonyl)benzaldehyde **4** as the sole product in 80% yield, while the expected CDC annulation product **5** was not obtained (eq. (1), Scheme 3). To our delight, substrate **4** was successfully converted to its CDC product **6** in 85% yield under the standard reaction conditions (eq. (1), Scheme 3). In addition, the CDC annulation of N-(2′-arylphenyl)formamides **7** was also workable and the desired phenanthridinones **8** were synthesized in moderate yields (eq. (2), Scheme 3). Finally, (1,1′-biphenyl)-2-yl formate **9** was also tested under the optimal reaction conditions. Unfortunately, a deesterification reaction mainly occurred while the CDC annulation product was not obtained (eq. (2), Scheme 3).

Table 2
Cu(0)/Selectfluor system-catalyzed cross-dehydrogenative coupling of **1** for the synthesis of **2**[a].



substrate (**1**)	product (**2**)/yield (%)[b]	substrate (**1**)	product (**2**)/yield (%)[b]
1a: X = H **1b**: X = ^{i}Pr **1c**: X = ^{t}Bu **1d**: X = Ph **1e**: X = F **1f**: X = Cl **1g**: X = Br **1h**: X = OCF_3	**2a**: 89% **2b**: 80% **2c**: 61% **2d**: 48% **2e**: 84% **2f**: 78% **2g**: 70% **2h**: 74%	**1n**	**2n**: 49%
		1o: X = H **1p**: X = F	**2o**: 87% **2p**: 95%
1i	**2i**: 45% **2i'**: 30%	**1q**: X = H **1r**: X = F **1s**: X= Cl	**2q**: 55% **2r**: 72% **2s**: 65%
1j	**2j**: 55% **2j'**: 33%	**1t**	**2t**: 78%
		1u	**2u**: 68%
1k	**2k**: 67%	**1v**	**2v**: 71%
1l: X = H **1m**: X = F	**2l**: 90% **2m**: 86%	**1w**	**2w**: 80%

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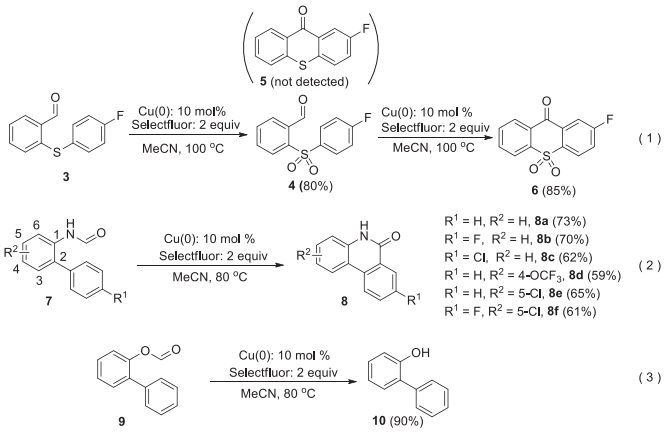
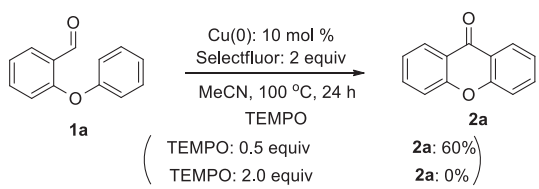


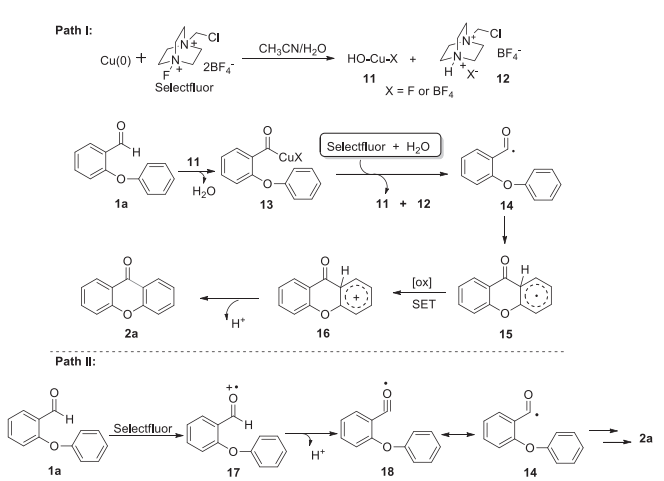
Scheme 3. The exploration of the Cu(0)/Selectfluor system for other CDC reactions.



Scheme 4. Mechanistic experiments.

Preliminary experiments were done to gain an insight into the mechanistic as shown in Scheme 4. The reaction was carried out in the presence of a radical scavenger TEMPO. When 2.0 equivalents of TEMPO were used, the reaction was almost depressed, suggesting that the reaction might involve a radical process [10].

On the basis of the mechanistic experiments and previous literature [5d,5f,8a-g,11,12], a plausible mechanism for the Cu(0)/Selectfluor system-catalyzed CDC annulation of **1a** is proposed in Scheme 5. Firstly, according to our previous research work, an active HOCu(II)X (X = F or BF_4) could be in situ generated from the redox reaction between Cu(0) and Selectfluor in the presence of water [8a-g]. Then HOCu(II)X abstracted a proton from the formyl group in **1a** to deliver intermediate **13** [8f]. **13** might be converted to radical species **14** along with the regeneration of **11** in the presence of Selectfluor and water. **14** underwent intramolecular radical cyclization to deliver intermediate **15** [5d,11]. Finally, oxidation of **15** followed by abstraction of one proton from the resulting **16** to produce **2a** (**Path I**) [5d,11]. Alternatively, since the single use of Selectfluor could also afford **2a** (see Table 1, entry 14), a mechanism involving Selectfluor-mediated radical pathway is also possible (**Path II**) [5d,5f,12].



Scheme 5. Proposed mechanism.

3. Conclusion

In conclusion, we have successfully developed an efficient method for the synthesis of xanthones from 2-aryloxybenzaldehydes involving the Cu(0)/Selectfluor system-catalyzed CDC annulation. The present protocol was further applied in other CDC annulations, thereby 9*H*-thioxanthen-9-one 10,10-dioxide and phenanthridin-6(5*H*)-ones were synthesized efficiently. The present methods has characteristic advantages of the use of inexpensive and low-toxic copper catalyst, relative mild reaction conditions (compared to most over 120 °C), and simple operation.

4. Experimental section

4.1. General methods

Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purifications. Melting points are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a spectrometer at 25 °C in $CDCl_3$ at 500 MHz and 125 MHz, respectively, with TMS as internal standard. Chemical shifts (δ) are expressed in ppm and coupling constants *J* are given in Hz. The IR spectra were recorded on an FT-IR spectrometer. GC-MS experiments were performed with EI source; high resolution mass spectra (HRMS) were obtained on a TOF MS instrument with ESI or EI source.

4.2. Preparation of the starting material 1 and 3

The starting material 2-aryloxybenzaldehydes **1** and 2-(*p*-fluorophenylthio)benzaldehyde **3** were synthesized according to the literature procedures [5b].

4.3. Typical experimental procedure for the synthesis of xanthones 2 from 1

1 (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol, 2 equiv), and MeCN (water content: 0.05 w/w %, 3 mL) were added to a 25-mL flask. Then the reaction mixture was stirred at 100 °C for 24 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100–200 mesh) using petroleum ether-EtOAc (20/1, V/V) as eluent to give pure **2**.

4.3.1. 9H-xanthen-9-one (2a) [13]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (52.4 mg, 89%); m.p. 180–182 °C (lit. [13] mp 179–180 °C); IR (neat): ν = 1654 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.37 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.77–7.74 (m, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.3, 156.3, 134.8, 126.8, 123.9, 121.9, 118.0.

4.3.2. 2-Isopropyl-9H-xanthen-9-one (2b)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a yellow oil (57.1 mg, 80%); IR (neat): ν = 1660 (C=

O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.37 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.20 (d, $J = 2.0$ Hz, 1H), 7.75–7.71 (m, 1H), 7.63 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.0$ Hz, 1H), 7.50 (d, $J = 8.0$ Hz, 1H), 7.45 (d, $J = 8.5$ Hz, 1H), 7.40–7.37 (m, 1H), 3.12–3.03 (m, 1H), 1.34 (d, $J = 7.0$ Hz, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.4, 156.2, 154.6, 144.7, 134.6, 133.8, 126.8, 123.7, 123.5, 121.9, 121.6, 118.0, 117.9, 33.7, 24.0; HRMS (ESI) for $C_{16}H_{15}O_2$ $[M+H]^+$: calcd. 239.1067, found 239.1061.

4.3.3. 2-(tert.-butyl)-9H-xanthen-9-one (**2c**) [14]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (46.2 mg, 61%); m.p. 110–112 °C (lit. [14] mp 114–115 °C); IR (neat): ν = 1659 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.36 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.34 (d, $J = 2.5$ Hz, 1H), 7.79 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.72–7.69 (m, 1H), 7.47 (d, $J = 9.0$ Hz, 1H), 7.43 (d, $J = 9.0$ Hz, 1H), 7.39–7.34 (m, 1H), 1.41 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.4, 156.2, 154.3, 147.1, 134.6, 132.7, 126.7, 123.7, 122.4, 121.9, 121.2, 117.9, 117.6, 34.7, 31.4.

4.3.4. 2-Phenyl-9H-xanthen-9-one (**2d**) [15]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (39.2 mg, 48%); m.p. 145–147 °C (lit. [15] mp 141–141.5 °C); IR (neat): ν = 1658 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.57 (d, $J = 2.5$ Hz, 1H), 8.38 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.97 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.5$ Hz, 1H), 7.76–7.72 (m, 1H), 7.70–7.68 (m, 2H), 7.57 (d, $J = 8.5$ Hz, 1H), 7.52–7.48 (m, 3H), 7.42–7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.2, 156.2, 155.5, 139.4, 137.0, 134.8, 133.6, 129.0, 127.7, 127.1, 126.8, 124.5, 124.0, 121.9, 121.8, 118.5, 118.0; HRMS (ESI) for $C_{19}H_{13}O_2$ $[M+H]^+$: calcd. 273.0910, found 273.0915.

4.3.5. 2-Fluoro-9H-xanthen-9-one (**2e**) [16]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (54.0 mg, 84%); m.p. 161–163 °C (lit. [16] m.p. 286–287 °C); IR (neat): ν = 1664 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.24 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.88 (dd, $J_1 = 8.5$ Hz, $J_2 = 3.0$ Hz, 1H), 7.69–7.66 (m, 1H), 7.42–7.36 (m, 3H), 7.33 (t, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.3 (d, $J = 2.5$ Hz), 159.6 (d, $J = 243.8$ Hz), 156.0, 152.2 (d, $J = 1.3$ Hz), 134.9, 126.5, 124.0, 122.8 (d, $J = 25$ Hz), 122.5 (d, $J = 7.5$ Hz), 120.9, 119.9 (d, $J = 7.5$ Hz), 117.9, 111.2 (d, $J = 23.8$ Hz).

4.3.6. 2-Chloro-9H-xanthen-9-one (**2f**) [7i]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (54.0 mg, 78%); m.p. 170–171 °C (lit. [7i] m.p. 169–171 °C); IR (neat): ν = 1664 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.26 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.21 (d, $J = 2.5$ Hz, 1H), 7.71–7.68 (m, 1H), 7.59 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.5$ Hz, 1H), 7.42 (d, $J = 8.0$ Hz, 1H), 7.38 (d, $J = 9.0$ Hz, 1H), 7.35 (t, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.9, 155.9, 154.4, 135.1, 134.8, 129.6, 126.7, 125.9, 124.2, 122.6, 121.3, 119.7, 117.9.

4.3.7. 2-Bromo-9H-xanthen-9-one (**2g**) [17]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (57.8 mg, 70%); m.p. 115–117 °C (lit. [17] m.p. 149.3–150.5 °C); IR (neat): ν = 1661 (C=O) cm^{-1}; ^1H NMR($CDCl_3$, 500 MHz): δ 8.44 (d, $J = 2.5$ Hz, 1H), 8.32 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.79 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.76–7.73 (m, 1H), 7.48 (d, $J = 8.5$ Hz, 1H), 7.41–7.38 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.9, 156.0, 154.9, 137.6, 135.2, 129.2, 126.8, 124.3, 123.1, 121.5, 120.0, 118.0, 117.0.

4.3.8. 2-(trifluoromethoxy)-9H-xanthen-9-one (**2h**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (62.2 mg, 74%); m.p. 101–103 °C; IR (neat): ν = 1667 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.27 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.13 (d, $J = 2.0$ Hz, 1H), 7.73–7.70 (m, 1H), 7.54 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.49 (d, $J = 9.0$ Hz, 1H), 7.45 (d, $J = 8.5$ Hz, 1H), 7.37 (t, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.1, 156.0, 154.1, 145.0, 135.2, 128.0, 126.7, 124.3, 122.4, 121.1, 120 (d, $J = 256.7$ Hz),120.0, 118.3, 118.0; HRMS (ESI) for $C_{14}H_8F_3O_3$ $[M+H]^+$: calcd. 281.0420, found 281.0416.

4.3.9. 1-Chloro-9H-xanthen-9-one (**2i**) [18]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (31.3 mg, 45%); m.p. 131–133 °C (lit. [18] m.p. 134–136 °C); IR (neat): ν = 1663 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.28 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.71–7.67 (m, 1H), 7.54 (t, $J = 8.0$ Hz, 1H), 7.42–7.34 (m, 4H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.8, 157.7, 154.9, 134.8, 134.4, 133.7, 127.0, 127.0, 124.2, 122.4, 118.9, 117.4, 117.2. Analytical data of another regioisomer *3-chloro-9H-xanthen-9-one (**2i′**)* [7f]: **2i′** was purified by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (20.8 mg, 30%); m.p. 129–130 °C (lit. [7f] m.p. 128.2–129.6 °C); IR (neat): ν = 1670 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.24 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.19 (d, $J = 8.5$ Hz, 1H), 7.69–7.65 (m, 1H), 7.40–7.37 (m, 2H), 7.35–7.31 (m, 1H), 7.27 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.0, 156.1, 155.9, 140.7, 134.9, 128.0, 126.6, 124.7, 124.2, 121.6, 120.3, 117.9, 117.8.

4.3.10. 1-Trifluoromethyl-9H-xanthen-9-one (**2j**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (43.6 mg, 55%); m.p. 173–175 °C; IR (neat): ν = 1673 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.32 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.81–7.72 (m, 4H), 7.47 (d, $J = 8.0$ Hz, 1H), 7.41–7.38 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.7, 157.6, 154.8, 135.0, 133.5, 129.3 (q, $J = 33.8$ Hz), 127.1, 124.5, 123.5 (q, $J = 7.5$ Hz), 123.3, 123.2 (q, $J = 272.5$ Hz), 122.5, 119.3, 117.4; HRMS (ESI) for $C_{14}H_8F_3O_2$ $[M+H]^+$: calcd. 265.0471, found 265.0467. Analytical data of another regioisomer *3-trifluoromethyl-9H-xanthen-9-one* (**2j′**): **2j′** was purified by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (26.2 mg, 33%); m.p. 91–93 °C; IR (neat): ν = 1675 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.44 (d, $J = 8.5$ Hz, 1H), 8.33 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.79–7.74 (m, 2H), 7.60 (d, $J = 8.5$ Hz, 1H), 7.51 (d, $J = 8.5$ Hz, 1H), 7.42 (t, $J = 7.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.3, 156.2, 155.6, 136.1 (q, $J = 32.5$ Hz), 135.5, 128.0, 126.8, 124.6, 123.9, 123.1 (q, $J = 271.3$ Hz), 121.8, 120.2 (q, $J = 3.8$ Hz), 118.1, 115.9 (q, $J = 3.8$ Hz); HRMS (ESI) for $C_{14}H_8F_3O_2$ $[M+H]^+$: calcd. 265.0471, found 265.0469.

4.3.11. 1-Fluoro-9H-xanthen-9-one (**2k**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (43.1 mg, 67%); m.p. 144–146 °C; IR (neat): ν = 1670 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.30 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.73–7.69 (m, 1H), 7.66–7.62 (m, 1H), 7.44 (d, $J = 8.0$ Hz, 1H), 7.40–7.36 (m, 1H), 7.28 (d, $J = 8.5$ Hz, 1H), 7.04–7.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.3 (d, $J = 1.3$ Hz), 161.5 (d, $J = 263.8$ Hz), 157.1 (d, $J = 3.8$ Hz), 155.3, 134.9, 134.7 (d, $J = 11.3$ Hz), 126.7, 124.2, 122.3, 117.6, 113.8 (d, $J = 3.8$ Hz), 112.4 (d, $J = 10$ Hz), 110.8 (d, $J = 21.3$ Hz); HRMS (ESI) for $C_{13}H_8FO_2$ $[M+H]^+$: calcd. 215.0503, found 215.0508.

4.3.12. 1-Chloro-9H-xanthen-9-one (**2l**) [18]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (62.3 mg, 90%). The structure of **2l** is the same as **2i**.

*4.3.13. 1-Chloro-7-fluoro-9H-xanthen-9-one (**2m**)*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (64.1 mg, 86%); m.p. 164–166 °C; IR (neat): $\nu = 1664$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 7.85–7.83 (m, 1H), 7.53 (t, $J = 8.0$ Hz, 1H), 7.38 (dd, $J_1 = 6.0$ Hz, $J_2 = 2.0$ Hz, 2H), 7.35 (d, $J = 8.5$ Hz, 1H), 7.32 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.9 (d, $J = 2.5$ Hz), 158.8 (d, $J = 245$ Hz), 157.6, 151.0 (d, $J = 1.3$ Hz), 134.4, 133.9, 127.2, 123.2 (d, $J = 7.5$ Hz), 122.8 (d, $J = 25$ Hz), 119.5 (d, $J = 7.5$ Hz), 118.0, 117.2, 111.6 (d, $J = 23.8$ Hz); HRMS (ESI) for $C_{13}H_7ClFO_2$ $[M+H]^+$: calcd. 249.0113, found 249.0118.

*4.3.14. 1-Phenoxy-9H-xanthen-9-one (**2n**)*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (42.4 mg, 49%); m.p. 132–134 °C; IR (neat): $\nu = 1661$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.29 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 7.71–7.67 (m, 1H), 7.58 (t, $J = 8.0$ Hz, 1H), 7.45 (d, $J = 7.5$ Hz, 1H), 7.40–7.33 (m, 3H), 7.25 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.0$ Hz, 1H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.09–7.05 (m, 2H), 6.80 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.7, 157.9, 157.5, 157.0, 155.2, 134.5, 134.5, 129.8, 126.9, 124.0, 123.6, 122.8, 118.9, 117.4, 114.7, 114.1, 112.9; HRMS (ESI) for $C_{19}H_{13}O_3$ $[M+H]^+$: calcd. 289.0859, found 289.0854.

*4.3.15. 2-Chloro-9H-xanthen-9-one (**2o**) [7i]*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (60.2 mg, 87%). The structure of **2o** is the same as **2f**.

*4.3.16. 2-Chloro-7-fluoro-9H-xanthen-9-one (**2p**)*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a pale yellow solid (70.9 mg, 95%); m.p. 195–197 °C; IR (neat): $\nu = 1667$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.22 (d, $J = 2.5$ Hz, 1H), 7.92–7.90 (m, 1H), 7.65 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.48–7.45 (m, 2H), 7.43 (d, $J = 8.5$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.3(d, $J = 1.3$ Hz), 158.9 (d, $J = 255$ Hz), 154.4, 152.2 (d, $J = 1.3$ Hz), 135.2, 130.0, 125.9, 123.3 (d, $J = 25$ Hz), 122.3 (d, $J = 6.3$ Hz), 121.8, 120.1 (d, $J = 8.8$ Hz), 119.8, 111.5 (d, $J = 22.5$ Hz);

*4.3.17. 2-Bromo-9H-xanthen-9-one (**2q**) [17]*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (45.4 mg, 55%). The structure of **2q** is the same as **2g**.

*4.3.18. 2-Bromo-7-fluoro-9H-xanthen-9-one (**2r**) [19]*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (63.4 mg, 72%); m.p. 183–185 °C (lit. [19] m.p. 181 °C); IR (neat): $\nu = 1656$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.40 (d, $J = 2.5$ Hz, 1H), 7.92 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.0$ Hz, 1H), 7.79 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.49–7.46 (m, 2H), 7.38 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 175.2 (d, $J = 1.3$ Hz), 158.9 (d, $J = 245.0$ Hz), 154.9, 152.2 (d, $J = 1.3$ Hz), 137.9, 129.1, 123.3 (d, $J = 25.0$ Hz), 122.4 (d, $J = 7.5$ Hz), 122.2, 120.1 (d, $J = 8.8$ Hz), 120.0, 117.3, 111.5 (d, $J = 23.8$ Hz).

*4.3.19. 2-Bromo-7-chloro-9H-xanthen-9-one (**2s**) [19]*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (60.4 mg, 65%); m.p. 217–219 °C (lit. [19] m.p. 210 °C); IR (neat): $\nu = 1668$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.41 (d, $J = 2.0$ Hz, 1H), 8.25 (d, $J = 2.5$ Hz, 1H), 7.81 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.67 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.45 (d, $J = 9.0$ Hz, 1H), 7.39 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.9, 154.8, 154.3, 138.0, 135.3, 130.2, 129.3, 126.1, 122.7, 122.4, 120.0, 119.8, 117.5.

*4.3.20. 3-Chloro-9H-xanthen-9-one (**2t**) [7f]*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (54.0 mg, 78%). The structure of **2t** is the same as **2i'**.

*4.3.21. 3-Bromo-9H-xanthen-9-one (**2u**)*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as a white solid (56.1 mg, 68%); m.p. 121–123 °C; IR (neat): $\nu = 1666$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.26 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.12 (d, $J = 8.5$ Hz, 1H), 7.70–7.67 (m, 1H), 7.59 (d, $J = 1.5$ Hz, 1H), 7.43 (dd, $J_1 = 8.5$ Hz, $J_2 = 2.0$ Hz, 1H), 7.40 (d, $J = 8.5$ Hz, 1H), 7.37–7.32 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.2, 156.0, 155.8, 135.0, 129.1, 128.0, 127.5, 126.6, 124.2, 121.7, 121.0, 120.6, 117.9; HRMS (ESI) for $C_{13}H_8BrO_2$ $[M+H]^+$: calcd. 274.9702, found 274.9706.

*4.3.22. 6-Bromo-2-(tert-butyl)-9H-xanthen-9-one (**2v**)*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (70.5 mg, 71%); m.p. 130–132 °C; IR (neat): $\nu = 1666$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.27 (d, $J = 2.5$ Hz, 1H), 8.15 (d, $J = 8.5$ Hz, 1H), 7.77 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.60 (d, $J = 2.0$ Hz, 1H), 7.43 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.5$ Hz, 1H), 7.36 (d, $J = 9.0$ Hz, 1H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.5, 156.1, 154.0, 147.5, 133.0, 128.8, 128.0, 127.3, 122.4, 121.0, 120.9, 120.6, 117.5; HRMS (ESI) for $C_{17}H_{16}BrO_2$ $[M+H]^+$: calcd. 331.0328, found 331.0324.

*4.3.23. 4-Chloro-9H-xanthen-9-one (**2w**) [20]*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (55.3 mg, 80%); m.p. 135–136 °C (lit. [20] m.p. 135–136 °C); IR (neat): $\nu = 1660$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.27 (dd, $J_1 = 8.0$ Hz, $J_2 = 1.5$ Hz, 1H), 8.20 (dd, $J_1 = 8.0$ Hz, $J_2 = 2.0$ Hz, 1H), 7.75–7.70 (m, 2H), 7.54 (d, $J = 8.0$ Hz, 1H), 7.40–7.35 (m, 1H), 7.27 (t, $J = 8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.4, 155.7, 151.7, 135.1, 134.9, 126.6, 125.2, 124.4, 123.8, 123.1, 122.8, 121.3, 118.2.

4.4. Typical experimental procedure for the synthesis of 6 from 4

2-(*p*-fluorophenylsulfonyl)benzaldehyde **4** (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol, 2 equiv), and MeCN (water content: 0.05 w/w %, 3 mL) were added to a 25-mL flask. Then the reaction mixture was stirred at 100 °C for 24 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100–200 mesh) using petroleum ether-EtOAc (20/1, V/V) as eluent to give pure **6**.

*4.4.1. 2-Fluoro-9H-thioxanthen-9-one 10,10-dioxide (**6**)*

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (66.9 mg, 85%); m.p. 235–236 °C; IR (neat): $\nu = 1674$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 8.35 (dd, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 8.22 (dd, $J_1 = 8.5$ Hz, $J_2 = 4.5$ Hz, 1H), 8.19 (dd, $J_1 = 7.5$ Hz, $J_2 = 1.0$ Hz, 1H), 8.01 (dd, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1H), 7.93–7.89 (m, 1H), 7.84–7.80 (m, 1H), 7.59–7.55 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.4, 165.1 (d, $J = 256.3$ Hz), 141.0, 137.2 (d, $J = 3.8$ Hz), 135.0, 133.5 (d, $J = 7.5$ Hz), 133.3, 130.4, 129.4, 126.7 (d, $J = 8.8$ Hz), 123.6, 122.1 (d, $J = 23.8$ Hz), 116.1 (d, $J = 23.8$ Hz); HRMS (ESI) for $C_{13}H_8FO_3S$ $[M+H]^+$: calcd. 263.0173, found 263.0177.

4.5. Typical experimental procedure for the synthesis of phenanthridinones 8 from 7

The starting material N-(2′-arylphenyl)formamide **7** were synthesized according to the literature procedures [21]. **7** (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol, 2 equiv), and MeCN (water content: 0.05 w/w %, 3 mL) were added to a 25-mL flask. Then the reaction mixture was stirred at 80 °C for 12 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100–200 mesh) using petroleum ether-EtOAc (20/1, V/V) as eluent to give pure **8**.

4.5.1. Phenanthridin-6(5H)-one (**8a**) [22]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (42.7 mg, 73%); m.p. 128–130 °C (lit. [22] m.p. 198 °C); IR (neat): $\nu = 1702$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.60 (s, 1H), 8.56 (d, $J = 6.0$ Hz, 1H), 7.92 (d, $J = 7.5$ Hz, 2H), 7.65–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 157.3, 137.6, 137.0, 127.7, 126.9, 126.0 (2C), 124.6, 124.2, 120.6, 119.7, 116.7, 109.8.

4.5.2. 8-Fluorophenanthridin-6(5H)-one (**8b**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (44.8 mg, 70%); m.p. 111–113 °C; IR (neat): $\nu = 1702$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.65–9.49 (m, 1H), 8.59–8.20 (m, 1H), 7.96–7.77 (m, 2H), 7.74–7.31 (m, 3H), 7.20–7.08 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 162.40 (d, $J = 250$ Hz), 157.3, 137.6, 127.4, 126.7, 125.5, 124.5, 122.1, 120.4, 116.7, 112.4 (d, $J = 23.8$ Hz), 109.9, 104.4 (d, $J = 22.5$ Hz); HRMS (ESI) for $C_{13}H_9FNO$ $[M+H]^+$: calcd. 214.0663, found 214.0667.

4.5.3. 8-Chlorophenanthridin-6(5H)-one (**8c**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (42.7 mg, 62%); m.p. 125–127 °C; IR (neat): $\nu = 1701$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ 9.56–9.51 (m, 1H), 8.54–8.51 (m, 1H), 7.93–7.76 (m, 2H), 7.69–7.55 (m, 1H), 7.48 (s, 1H), 7.42 (t, $J = 7.5$ Hz, 1H), 7.36 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 157.2, 137.4, 133.4, 127.3, 125.3, 124.6, 121.4, 120.7, 120.4, 119.7, 117.0, 110.4, 109.9; HRMS (ESI) for $C_{13}H_9ClNO$ $[M+H]^+$: calcd. 230.0367, found 230.0361.

4.5.4. 2-(trifluoromethoxy)phenanthridin-6(5H)-one (**8d**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (49.2 mg, 59%); m.p. 87.3–88.2 °C; IR (neat): $\nu = 1665$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 9.69 (s, 1H), 8.61 (s, 1H), 8.00 (d, $J = 6.2$ Hz, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 7.56 (s, 1H), 7.48 (t, $J = 7.5$ Hz, 1H), 7.39 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (DMSO, 100 MHz): δ 160.2, 145.39, 145.37, 128.8, 128.5, 124.6, 121.6, 120.8, 120.7 (q, $J = 254.0$ Hz), 117.4, 116.3, 113.9, 113.3, 111.9; HRMS (ESI) for $C_{14}H_9F_3NO_2$ $[M+H]^+$: calcd. 280.0580, found 280.0587.

4.5.5. 3-Chlorophenanthridin-6(5H)-one (**8e**) [23]

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (44.8 mg, 65%); m.p. 261–263 °C (lit. [23] m.p. 280–282 °C); IR (neat): $\nu = 1677$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 9.64 (s, 1H), 8.61-8.56 (m, 1H), 7.95 (s, 1H), 7.88 (s, 1H), 7.71 (s, 1H), 7.52 (s, 1H), 7.45 (t, $J = 7.5$ Hz, 1H), 7.41 (d, $J = 8.2$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.3, 137.5, 133.5, 127.3, 125.4, 125.2, 124.7, 121.5, 120.8, 120.5, 117.1, 110.5, 110.0.

4.5.6. 3-Chloro-8-fluorophenanthridin-6(5H)-one (**8f**)

Purification by column chromatography (petroleum ether/EtOAc, 20/1) as white solid (45.3 mg, 61%); m.p. 184.3–186.2 °C; IR (neat): $\nu = 1659$ (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 9.56 (s, 1H), 8.60-8.30 (m, 1H), 7.89-7.41 (m, 4H), 7.19 (td, $J_1 = 8.8$ Hz, $J_2 = 2.1$ Hz, 1H); ^{13}C NMR (DMSO, 100 MHz): δ 162.1 (d, $J = 242.2$ Hz), 160.5, 139.0, 137.6, 131.8 (2C), 124.8, 122.5, 121.9, 115.9, 112.3, 103.5 (d, $J = 26.0$ Hz), 99.9 (d, $J = 22.3$ Hz); HRMS (ESI) for $C_{13}H_8ClFNO$ $[M+H]^+$: calcd. 248.0273, found 248.0268.

4.6. Mechanistic studies

4.6.1. Effect of radical scavenger TEMPO on the formation of 2a

Procedure: To a 25 mL Schlenk flask, **1a** (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol, 2 equiv), TEMPO (0.15 mmol, or 0.6 mmol), and MeCN (water content: 0.05 w/w %, 3 mL) were added. The solution was then stirred at 130 °C for 8 h. After completion of the reaction as indicated by TLC, the mixture was sent for GC analysis (TEMPO: 0.5 equiv, **2a**: 60%; TEMPO = 2.0 equiv, **2a**: 0%).

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Appendix A. Supplementary data

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References

[1] (a) For selected reviews on cross coupling reactions for C-C bond formation, see: F.S. Han Chem. Soc. Rev. 42 (2013) 5270;
(b) S.M. Roberts, Metal-catalysed Carbon-Carbon Forming Reactions, vol. 3, John Wiley, Chichester, Hoboken, 2004;
(c) A. Biffis, P. Centomo, A. Del Zotto, M. Zecca, Chem. Rev. 118 (2018) 2249;
(d) R. Chinchilla, C. Nájera, Chem. Rev. 107 (2007) 874;
(e) R. Jana, T.P. Pathak, M.S. Sigman, Chem. Rev. 111 (2011) 1417;
(f) C.C. Johansson Seechurn, M.O. Kitching, T.J. Colacot, V. Snieckus, Angew. Chem. Int. Ed. 51 (2012) 5062.

[2] (a) For selected reviews on cross coupling reactions for C-X (X = heteroatoms) bond formation, see: K.M. Korch, D.A. Watson Chem. Rev. (2019) https://doi.org/10.1021/acs.chemrev.8bpp628. APAS article(and references cited therein);
(b) J.F. Hartig, Angew. Chem. Int. Ed. 37 (1998) 2046;
(c) P. Ruiz-Castillo, S.L. Buchwald, Chem. Rev. 116 (2016) 12564.

[3] (a) For selected reviews, see: C.-L. Sun, B.-J. Li, Z.-J. Shi Chem. Commun. 46 (2010) 677;
(b) H. Yi, G. Zhang, H. Wang, Z. Huang, J. Wang, A.K. Singh, A. Lei, Chem. Rev. 117 (2017) 9016;
(c) X. Chen, K.-M. Engle, D.-H. Wang, J.-Q. Yu, Angew. Chem. Int. Ed. 48 (2009) 5094;
(d) J. Wencel-Delord, E. Dröge, F. Glorius, Chem. Soc. Rev. 40 (2011) 4740;
(e) D.Y.-K. Chen, S.W. Youn, Chem. Eur. J. 18 (2012) 9452;
(f) J. Yamaguchi, A.D. Yamaguchi, K. Itami, Angew. Chem. Int. Ed. 51 (2012) 8969;
(g) T. Brückl, R.D. Baxter, Y. Ishihara, P.S. Baran, Acc. Chem. Res. 45 (2012) 826.

[4] (a) C.J. Li, Acc. Chem. Res. 42 (2009) 335;
(b) S.A. Girard, T. Knauber, C.J. Li, Angew. Chem. Int. Ed. 53 (2014) 74;
(c) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi, A. Lei, Chem. Rev. 115 (2015) 12138;
(d) C.S. Yeung, V.M. Dong, Chem. Rev. 111 (2011) 1215;
(e) H. Wang, X. Ga, Z. Lv, T. Abdeliah, A. Lei, Chem. Rev. 119 (2019) 6769 (and references cited therein).

[5] (a) P. Wang, H. Rao, R. Hua, C.-J. Li, Org. Lett. 14 (2012) 902;
(b) S. Wertz, D. Leifert, A. Studer, Org. Lett. 15 (2013) 928;
(c) S.K. Manna, S.L.K. Manda, G. Panda, Tetrahedron Lett. 55 (2014) 5759;
(d) H. Rao, X. Ma, Q. Liu, Z. Li, S. Cao, C.-J. Li, Adv. Synth. Catal. 355 (2013) 2191;
(e) J.B. Singh, K. Mishra, T. Gupta, R.M. Singh, ChemistrySelect 2 (2017) 1207;
(f) J. Tang, S. Zhao, Y. Wei, Z. Quan, C. Huo, Org. Biomol. Chem. 15 (2017) 1589.

[6] (a) Y. Sakagami, in: I. Ahmad, F. Aqil, M. Qwais (Eds.), Modern Phytomedicine: Tuning Medicinal Plants into Drugs, Wiley-VCH, Weiheim, 2006, pp. 138–153;
(b) J.C. Roberts, Chem. Rev. 61 (1961) 591;
(c) N.H. Daud, C.S. Aung, A.K. Hewavitharana, A.S. Wilkinson, J. Pierson, S.J. Roberts-Thomson, P.N. Shaw, G.R. Monteith, M.J. Gidley, M. Parat, J. Agric. Food Chem. 58 (2010) 5181;
(d) S.M. Kupchan, D.R. Streelman, A.T. Sneden, J. Nat. Prod. 43 (1980) 296.

[7] (a) C.M.G. Azevedo, C.M.M. Afonso, M.M.M. Pinto, Curr. Org. Chem. 16 (2012) 2818;
(b) J.S. Yadav, Pure Appl. Chem. 65 (1993) 1349;
(c) W. Jackson, R. Boyd, L. Froelich, D. Gapinski, B. Mallett, J. Sawyer, J. Med. Chem. 36 (1993) 1726;
(d) G.A. Olah, T. Mathew, M. Farnia, G.K.S. Prakash, Synlett (1999) 1067;
(e) K. Lan, S. Fen, Z.X. Shan, Aust. J. Chem. 60 (2007) 80;
(f) J. Li, C. Jin, W. Su, Heterocycles 83 (2011) 855;
(g) M. Pickert, A.W. Frahm, Arch. Pharm. Pharm. Mecd. Chem. 331 (1998) 177;
(h) R.K.M. Pillai, P. Naiksatam, F. Johnson, R. Rajagopalan, P.C. Watts, R. Cricchio, S. Borras, J. Org. Chem. 51 (1986) 711;
(i) C. Zhou, R.C. Larock, J. Org. Chem. 71 (2006) 3551;
(j) D. Zhu, M. Li, Z. Wu, Y. Du, B. Luo, P. Huang, S. Wen, Eur. J. Org. Chem. (2019) 4566;
(k) J.L. Bachman, P.R. Escamilla, A.J. Boley, C.I. Pavlich, E.V. Anslyn, Org. Lett. 21 (2019) 206;
(l) C.M.M. Santos, M. Freitas, E. Fernandes, Eur. J. Med. Chem. 157 (2018) 1460;
(m) C. Fernandes, M.L. Carraro, J. Ribeiro, J. Araújo, M.Z. Tiritan, M.M.M. Pinto, Molecules 24 (2019) 791.

[8] (a) W. Zhang, J. Zhang, Y. Liu, Z. Xu, Synlett 24 (2013) 2709;
(b) J. Zhang, D. Wu, X. Chen, Y. Liu, Z. Xu, J. Org. Chem. 79 (2014) 4799;
(c) J. Zhang, H. Wang, S. Ren, W. Zhang, Y. Liu, Org. Lett. 17 (2015) 2920;
(d) H. Bao, Z. Xu, D. Wu, H. Zhang, H. Jin, Y. Liu, J. Org. Chem. 82 (2017) 109;
(e) J. Zhang, H. Zhang, D. Shi, H. Jin, Y. Liu, Eur. J. Org. Chem. (2016) 5545;
(f) S. Ren, J. Zhang, H. Wang, W. Zhang, Y. Liu, M. Liu, Eur. J. Org. Chem. (2015) 5381;
(g) J. Zhang, D. Shi, H. Zhang, Z. Xu, H. Bao, H. Jin, Y. Liu, Tetrahedron 73 (2017) 154;
(h) H. Bao, B. Zhou, H. Jin, Y. Liu, J. Org. Chem. 84 (2019) 3579;
(i) B. Zhou, L. Zheng, H. Jin, Q. Wu, T. Li, Y. Liu, ChemistrySelect 3 (2018) 7354;
(j) B. Zhou, Q. Liu, H. Wang, H. Jin, Y. Liu, Tetradedron 75 (2019) 3815;
(k) H. Bao, B. Zhou, H. Jin, Y. Liu, Org. Biomol. Chem. 17 (2019) 5021.

[9] (a) X.-X. Guo, D.-W. Gu, Z. Wu, W. Zhang, Chem. Rev. 115 (2015) 1622;
(b) J. Liu, G. Chen, Z. Tan, Adv. Synth. Catal. 358 (2016) 1174;
(c) W.-H. Rao, B.-F. Shi, Org. Chem. Front. 3 (2016) 1028;
(d) J.-L. Hu, J. Li, Y.-F. Zhou, Curr. Green Chem. 2 (2015) 170;
(e) R. Gephart, T.H. Warren, Organometallics 31 (2012) 7728;
(f) Z.-K. Li, X.-S. Jia, Y. Liang, Synthesis 50 (2018) 4165;
(g) A.E. Wendlandt, A.M. Suess, S.S. Stahl, Angew. Chem. Int. Ed. 50 (2011) 11062.

[10] (a) P.A. Sibbald, F.E. Michael, Org. Lett. 11 (2009) 1147;
(b) A.C. Albéniz, P. Espinet, R. López-Fernández, A. Sen, J. Am. Chem. Soc. 124 (2002) 11278.

[11] (a) Z. Li, Y. Zhang, L. Zhang, Z.-Q. Liu, Org. Lett. 16 (2014) 382;
(b) Z. Li, F. Fan, J. Yang, Z.-Q. Liu, Org. Lett. 16 (2014) 3396;
(c) M. Nishino, K. Hirano, T. Satoh, M. Miura, J. Org. Chem. 76 (2011) 6447;
(d) S.L. Zhou, L.-N. Guo, S. Wang, X.-H. Duan, Chem. Commun. 50 (2014) 3589;
(e) Z.-Q. Zhu, T.-T. Wang, P. Bai, Z.-Z. Huang, Org. Biomol. Chem. 12 (2014) 5839.

[12] Y. Lv, X. Wang, H. Cui, K. Sun, W. Pu, G. Li, Y. Wu, J. He, X. Ren, RSC Adv. 6 (2016) 74917.

[13] R. Giri, J.R. Goodell, C. Xing, A. Benoit, H. Kaur, H. Hiasa, D.M. Ferguson, Bioorg. Med. Chem. 18 (2010) 1456.

[14] M. Kulka, J. Am. Chem. Soc. 76 (1954) 5469.

[15] C.S. Schoepfle, J.H. Truesdail, J. Am. Chem. Soc. 59 (1937) 372.

[16] M. Mao, Q.-Q. Wu, M.-G. Ren, Q.-H. Song, Org. Biomol. Chem. 9 (2011) 3165.

[17] M.K.J. ter Wiel, B.L. Feringa, Tetrahedron 65 (2009) 4332.

[18] L. Hintermann, R. Masuo, K. Suzuki, Org. Lett. 10 (2008) 4859.

[19] I. Granoth, H.J. Pownall, J. Org. Chem. 40 (1975) 2088.

[20] J.F. Bunnet, T. Kato, R.R. Flynn, J. Org. Chem. 28 (1963) 1.

[21] C. Wan, J. Zhao, M. Xu, J. Huang, J. Org. Chem. 79 (2014) 4751.

[22] S. Goswami, A.K. Adak, R. Mukherjee, S. Jana, S. Dey, J.F. Gallagher, Tetrahedron 61 (2005) 4289.

[23] Y. Chen, Y. Wu, Y. Jhan, J. Hsieh, Org. Chem. Front. 1 (2014) 253.

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