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Graphical Abstract

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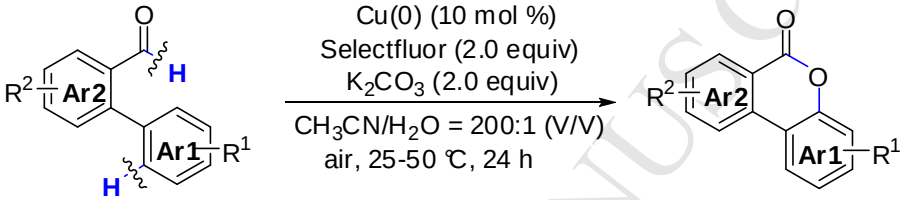

Ar1 = aryl; Ar2 = aryl or pyrazolyl

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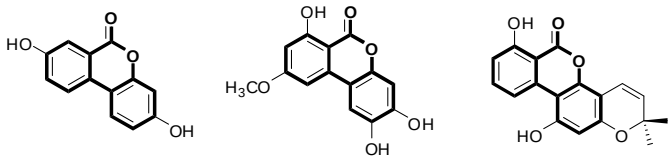
ABSTRACT

A mild and efficient protocol for the synthesis of dibenzopyranones and pyrazolobenzopyranones was developed involving a copper(0)/Selectfluor system-catalyzed double C-H activation/oxygen insertion of 2-arylbenzaldehydes and 5-arylpyrazole-4-carbaldehydes. Preliminary mechanistic studies suggest that both water and dioxygen act as the oxygen source in the formation of pyranone scaffolds.

1. Introduction

Dibenzopyranone scaffold is the key structure in a number of natural products which display unique biological activities.[1] For example, Urolithin A (Figure 1-a) was known to effectively inhibit cancer cell proliferation;[1a] Atenuisol (Figure 1-b) was disclosed to show the high correlation with FabI-inhibition and whole cell antibacterial activity;[1b] Sarolactone (Figure 1-c), a compound isolated from *Hypericum japonicum*, was found to exhibit antimicrobial properties.[1c] Besides, dibenzopyranones can serve as useful intermediates for the synthesis of many pharmaceutically interesting compounds[2] as well as functional molecules in materials science.[3] Thus, the development of efficient methods for the preparation of dibenzopyranones has received increasingly attention in the past decades.[4-10] Typically, dibenzopyranones are synthesized through Baeyer-Villiger oxidation of fluorenones (Scheme 1, path a)[4] or by oxidation of benzylic C-H bonds in 6*H*-benzo[*c*]chromenes (Scheme 1, path b).[5] Alternative methods include cross-coupling of aryl *o*-benzoates (Scheme 1, path c),[6] palladium-catalyzed C-H activation/carbonylation of 2-arylphenols (Scheme 1, path d),[7] intramolecular lactonization of 2-halobiarylcarboxylic acid derivatives (Scheme 1, path e),[8] tandem Suziki-Miyaura cross-coupling/lactonization between 2-halobenzaldehydes and *o*-hydroxyarylboronic acids (Scheme 1, path f),[9] and others.[10]

Despite much progress being made for the synthesis of dibenzopyranones, most of the existing methods suffer from one or more limitations including the use of prefunctionalized precursors, expensive catalysts, multistep procedures, the requirement of high or low temperature, and the employment of toxic reagents. Therefore, it is highly desirable to develop novel methods for the synthesis of dibenzopyranones from easily available starting materials using inexpensive catalysts under mild reaction conditions.



(a) Urolithin A (b) Altenuisol (c) Sarolactone

Figure 1. Bioactive compounds containing dibenzopyranone scaffold

As part of our research interest in developing mild and efficient catalyst systems for the construction of useful molecules,[11] we have recently disclosed that the combination of copper powder and Selectfluor may generate an active XCuOH species (X = F or BF_4) which is easily able to undergo oxycupration toward carbon-carbon multiple bonds and induce

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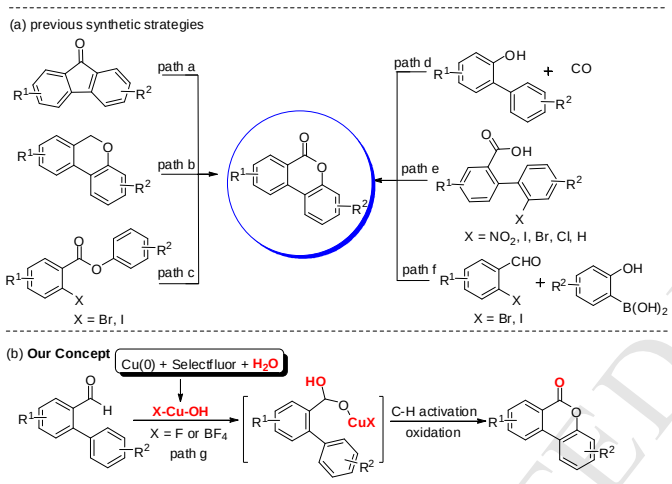
successive tandem reactions.[11a-c] For example, in 2014, we reported a Cu(0)/Selectfluor system-catalyzed concise synthesis of 3-formyl-1-indenones from 1,5-enynes involving a cyclization/carbon-carbon bond cleavage sequence in which double oxycuprations of 1,5-enynes were thought to be the key steps.[11b] In 2015, we described a Cu(0)/Selectfluor system-catalyzed facile synthesis of fluorinated fluorenones from 1,6-enynes involving an oxycupration-triggered annulation/fluorination sequence.[11c] Inspired by the finding that the XCuOH species can easily undergo oxycupration toward carbon-carbon multiple bonds, we envisioned that it may undergo oxycupration toward C=O bonds as well. On the basis of this assumption, it is reasonable to expect that dibenzopyranones might be synthesized from 2-arylbenzaldehydes through an oxycupration/C-H activation/oxidation sequence (Scheme 1, path g). Herein we described our concept for the direct synthesis of dibenzopyranones from 2-arylbenzaldehydes using the Cu(0)/Selectfluor catalytic system as well as the related mechanism studies. When our work approached completion, Ray *et al.*[12] reported a CuCl/TBHP system-catalyzed direct transformation of 2-arylbenzaldehydes to dibenzopyranones in which 6 equivalents of TBHP act as the oxygen source for the formation of pyranone scaffolds.



Scheme 1. Strategies for the synthesis of dibenzopyranones

2. Results and discussion

We commenced the study with 2-phenylbenzaldehyde **1a** as the model substrate, and the screening results are listed in Table 1. When **1a** was treated with Cu(0) powder (10 mol %), Selectfluor (2.0 equiv), and $NaHCO_3$ (2.0 equiv) in CH_3CN/H_2O (200/1, V/V) at 25 ºC for 24 h, dibenzopyranone **2a** was indeed obtained in 46% yield (entry 1, Table 1). Switching the base from $NaHCO_3$ to K_2CO_3, the reaction proceeded more smoothly to give **2a** in 92% yield (entry 2, Table 1). Several other bases (Na_2CO_3, $KHCO_3$, and Et_3N) were investigated, and it was found that the reaction failed to give the desired product **2a** (entries 3-5, Table 1). The catalytic activity of a series of copper and iron salts were studied for the reaction, and it was found that their catalytic performances were inferior to that of Cu(0) powder (entries 6-13 vs 2, Table 1). Among several solvent systems investigated so far, a combined solvent CH_3CN/H_2O = 200:1 (V/V) has proved to be the most suitable medium for the reaction (entries 14-18 vs 2, Table 1). Controlled experiments indicated that either the Cu(0) powder or Selectfluor was indispensable for the reaction (entries 19, 20 vs 2, Table 1). Using 2.0 equivalents of Selectfluor is just fine for the reaction while the excessive or deficient use of Seletfluor would lead to a lower yield of **2a** (entry 21 vs 2, Table 1). An attempt to use catalytic amounts of Selectfluor in the presence of dioxygen gas (balloon, 1 atm) only gave a low yield of **2a** (25%, entry 22, Table 1). When Selectfluor was replaced with NFSI (*N*-fluorobenzenesulfonimide), the reaction did not take place and the starting material **1a** was recovered (entry 23, Table 1). Note that the use of 2 equivalents of K_2CO_3 is necessary for the reaction otherwise a lower yield of **2a** would be obtained (entry 24 vs 2, Table 1). It was found that increasing the reaction temperature gave a negative effect on the yield of **2a** (entry 25 vs 2, Table 1).

With the optimized reaction conditions in hand, we then investigated the substrate scope of the Cu(0)/Selectfluor system-catalyzed double C-H activation/oxygen insertion of 2-arylbenzaldehydes (Table 2). As shown in Table 2, a range of 2-arylbenzaldehydes **1** with various substituents could be converted to dibenzopyranones **2** in moderate to good yields (31-87%, Table 2). Generally, both electron-donating and –withdrawing substituents in the aryl ring of **1** were compatible with the reaction conditions, among which include methyl, methoxy, *tert*-butyl, halo (F, Cl, Br) and OCF_3 groups. It was found that the electronic nature of R^1 has a significant effect on the reaction outcome in terms of the yield. For instance, when R^1 represents electron-withdrawing group (e.g. F, Cl, Br, and OCF_3), the reaction proceeded more smoothly and gave higher yield of product in comparison with those cases that R^1 is electron-donating group (**2b**-**2e** vs **2f**; **2h**-**2k** vs **2l**, Table 2). In contrast, it seemed that the electronic property of R^2 has little effect on the reaction outcome (**2h**, **2m**, **2n**, **2s**, **2v** except **2t**, Table 2). When **1k** was used, the reaction proceeded more smoothly by using CuCl as the catalyst instead of the Cu(0) powder, and the desired product **2k** was obtained in 70% yield (**1k**, Table 2). For substrate **1u**, it is noteworthy that 50 ºC is a required temperature for a better yield of **2u** (50%, Table 2). Interestingly, when 2'-chlorobiphenyl-2-carbaldehyde **1w** was used, the reaction underwent a competitive cross-dechlorinative C-O coupling reaction to give a dibenzopyranone **2a** in 67% yield while the desired product **2w** from the normal cross-dehydrogenative C-O coupling reaction was not detected (**1w**, Table 2).

Although there are a number of literatures on the synthesis of dibenzopyranones,[4-10,12] to the best of our knowledge, very few have focused on the synthesis of heterocyclobenzopyranones.[13] To broaden the synthetic application of the present method, we next attempted to synthesize heterocyclobenzopyranones. We commenced the study with substrates **3** containing pyrazole moieties due to the potential utilities of pyrazole derivatives in chemical, materials science and pharmaceutical fields.[14] It was found that the reaction generally required a higher temperature

Table 1. Optimization of reaction conditions[a]

Entry	Catalyst	Oxidant	Base	Solvent	Yield %
1	Cu	Selectfluor	$NaHCO_3$	CH_3CN/H_2O = 200:1	46
2	**Cu**	**Selectfluor**	**K_2CO_3**	**CH_3CN/H_2O = 200:1**	**92(86)[c]**
3	Cu	Selectfluor	Na_2CO_3	CH_3CN/H_2O = 200:1	n.r.
4	Cu	Selectfluor	$KHCO_3$	CH_3CN/H_2O = 200:1	trace

5	Cu	Selectfluor	EtN_3	CH_3CN/H_2O = 200:1	trace
6	CuI	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	20
7	CuBr	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	30
8	CuCl	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	85
9	$CuCl_2$	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	70
10	$Cu(OAc)_2$	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	78
11	$Cu(NO_3)_2$	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	82
12	$CuSO_4$	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	25
13	$FeCl_2$	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	n.r.
14	Cu	Selectfluor	K_2CO_3	$DMSO/H_2O$ = 200:1	n.r.
15	Cu	Selectfluor	K_2CO_3	dioxane/H_2O = 200:1	n.r.
16	Cu	Selectfluor	K_2CO_3	DCE/H_2O = 200:1[d]	n.r.
17	Cu	Selectfluor	K_2CO_3	CH_3CN/H_2O = 100:1	88
18	Cu	Selectfluor	K_2CO_3	CH_3CN/H_2O = 500:1	89
19	--	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	n.r.
20	Cu	--	K_2CO_3	CH_3CN/H_2O = 200:1	n.r.
21	Cu	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	17[e], 70[f]
22	Cu	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	25[g]
23	Cu	NFSI[h]	K_2CO_3	CH_3CN/H_2O = 200:1	n.r.
24	Cu	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	72[i], 75[j]
25	Cu	Selectfluor	K_2CO_3	CH_3CN/H_2O = 200:1	60[k], 66[l]

[a]Reaction condiitons: **1a** (0.3 mmol), catalyst (10 mol %), oxidant (2.0 equiv), solvent (3 mL) at 25 ºC for 24 h unless otherwise noted.

[b]Determined by GC using dodecane as an internal standard.

[c]Isolated yield.

[d]DCE: 1, 2-dichloroethane.

[e,f]1.0 and 3.0 equivalents of Selectfluor were used, respectively.

[g]Using 0.3 equivalents of Selectfluor in the presence of O_2 (balloon, 1 atm).

[h]NFSI: *N*-fluorobenzenesulfonimide.

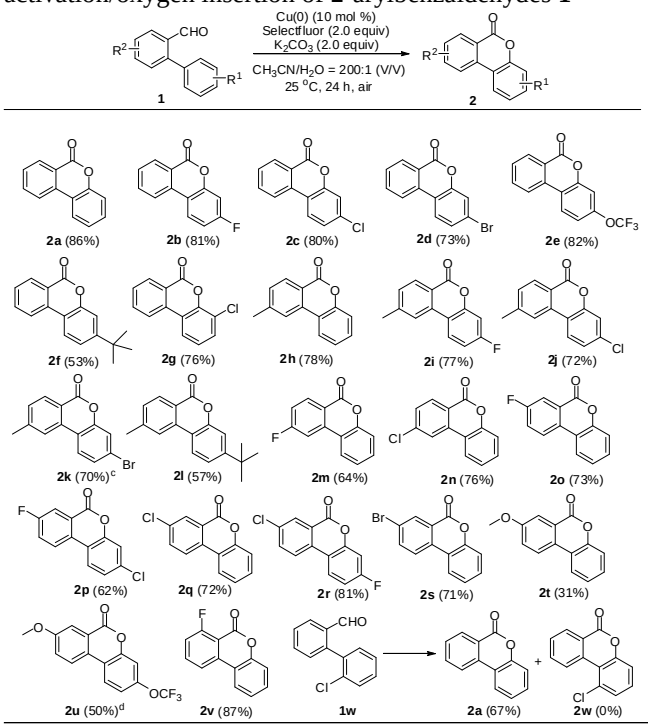
[i,j]Using 0.5 and 1.0 equivalents of K_2CO_3, respectively..

[k,l]The reaction temperature is 50 and 80 °C, respectively.

(50 ºC) for the efficient formation of **4** in comparison with the lactonization of **1** (Table 3 vs Table 2). Under the slightly modified reaction conditions, a range of 3-methyl-1,5-diphenyl-1*H*-pyrazole-4-carbaldehydes (**3a**-**3e**) could be intramolecularly lactonized to pyrazolobenzopyranones **4** in moderate to good yields catalyzed by the Cu(0)/Selectfluor system (55-72%, **4a**-**4e**, Table 3). For substrate **3** possessing two phenyl rings adjacent to the formyl group, the cross-dehydrogenative C-O coupling reaction predominantly took place in the phenyl ring substituted with more strong electron-withdrawing groups (**4g**-**4j**, Table 3). When **3f** was used as the substrate, the reaction gave a regioisomeric mixture of **4f** and **4f'** in a total yield of 62% with a molar ratio of 1:0.41 determined by NMR analyses (**3f**, Table 3; see in the Supporting Information). Similarly, the intramolecular lactonization of **3k** resulted in a regioisomeric mixture of **4k** and **4k'** in a total yield of 63% with a molar ratio of 1:0.94 (**3k**, Table 3; see in the Supporting Information).

To further demonstrate the synthetic potential of the present method, the intramolecular lactonization of **1a** at the gram-scale was also carried out (eq. 1, Scheme 2). Thus, 1.8 g of **1a** (10 mmol) could give 1.49 g of **2a** in a yield of 76% under the standard reaction conditions (eq. 1, Scheme 2). In addition, to demonstrate the synthetic value of dibenzopyranones **2**, the application of **2a** as a synthetic intermediate in the synthesis of 2'-hydroxybiphenyl-2-carboxylic acid **5**, 6*H*-benzo[*c*]chromene **6**, and 6-phenyl-6*H*-benzo[*c*]chromen-6-ol **7**. was carried out. Thus, treatment of **2a** with 5% (W/W) NaOH solution in acetonitrile for 6 h afforded **5** in 98% yield (eq. 2, Scheme 2);[15] the reduction of **2a** with $NaBH_4$ in ethanol for 3 h gave **6** in 92% yield (eq. 3, Scheme 2);[16] the nucleophilic addition of PhMgBr to **2a** in THF delivered **7** in 94% yield (eq. 4, Scheme 2).[17]

Table 2. Investigation of substrate scope in the Cu(0)/Selecfluor system-catalyzed double C-H activation/oxygen insertion of 2-arylbenzaldehydes **1**[a,b]



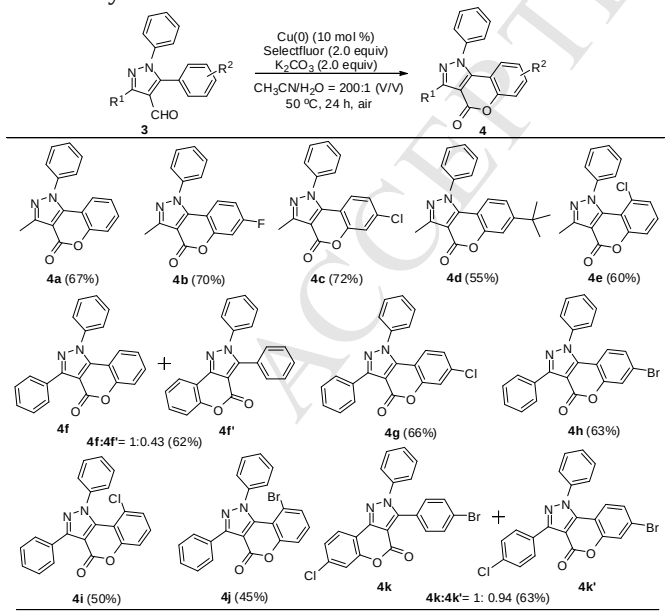
[a]All reactions were carried out with **1** (0.3 mmol), Cu(0) (10 mol % based on **1**), Selectfluor (2.0 equiv), and K_2CO_3 (2.0 equiv) in solvent (CH_3CN/H_2O = 200:1 (V/V), 3 mL) at 25 ºC for 24 h unless otherwise noted.

[b]Isolated yield.

[c]Cu(0) powder was replaced with CuCl as the catalyst.

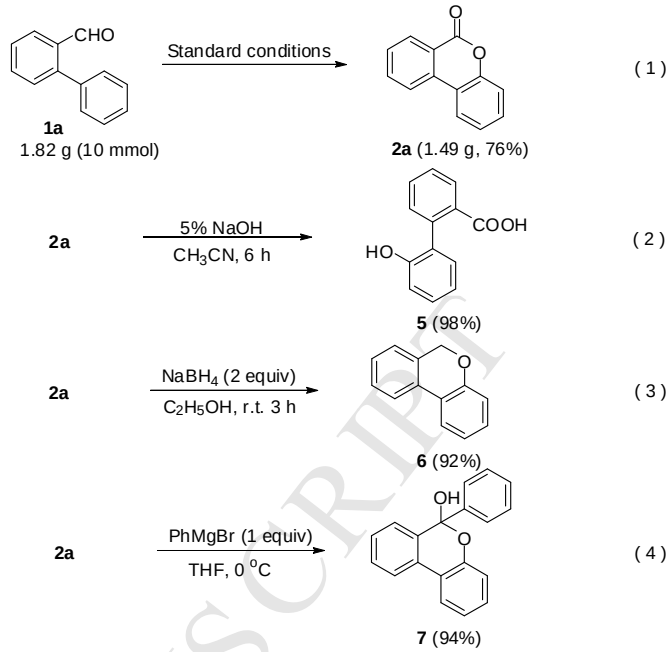
[d]The reaction temperature is 50 ºC.

Table 3. Cu(0)/Selecfluor system-catalyzed double C-H activation/oxygen insertion of 5-arylpyrazole-4-carbaldehydes **3**[a,b]



[a]All reactions were carried out with **1** (0.3 mmol), Cu(0) (10 mol % based on **1**), Selectfluor (2.0 equiv), and K_2CO_3 (2.0 equiv) in solvent (CH_3CN/H_2O = 200:1 (V/V), 3 mL) at 50 ºC for 24 h unless otherwise noted.

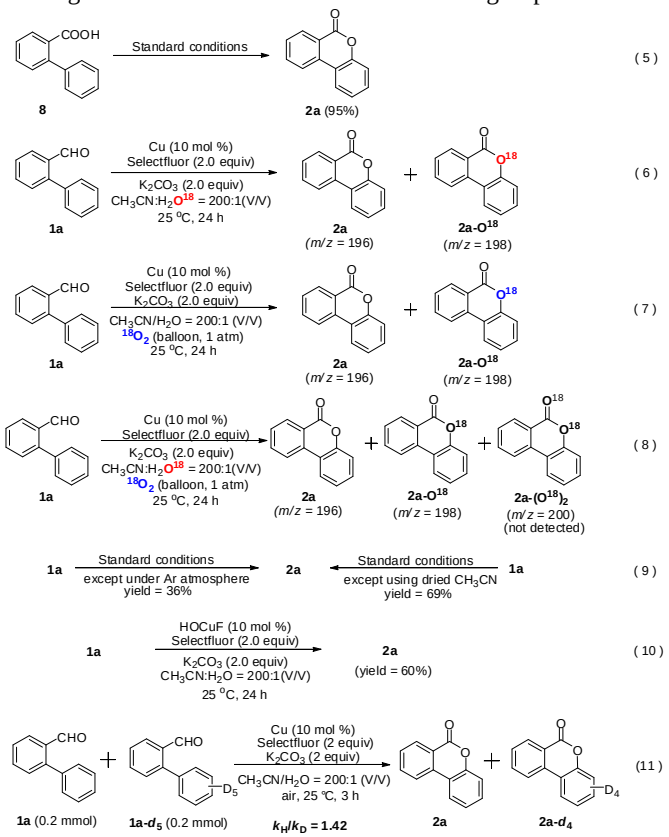
[b]Isolated yields.



Scheme 2. Gram-scale synthesis of **2a** and its synthetic applications

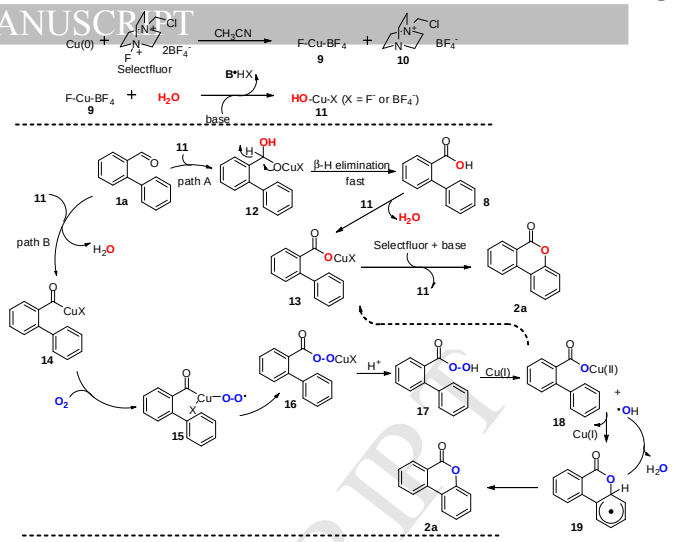
To elucidate the mechanism of the double C-H activation/oxygen insertion of 2-arylbenzaldehydes, some mechanistic experiments were carried out (Scheme 3). According to our initial assumption (path g, Scheme 1), we believed that 2-arylbenzoic acid might be an intermediate for the intramolecular lactonization of **1**. When the preparative 2-phenylbenzoic acid **8**[8k] was subjected to the standard reaction conditions, **2a** was indeed obtained in 95% yield (eq. 5, Scheme 3). When **1a** reacted under the standard reaction conditions except using a CH_3CN/H_2O^{18} = 200:1 (V/V) solvent system, the O^{18}-incorporated product **2a-O^{18}** (m/z = 198) was detected (eq. 6, Scheme 3; also see Figure S1, Supporting Information). On the other hand, when **1a** was subjected to the standard reaction conditions except in the presence of an $^{18}O_2$ atmosphere (balloon, 1 atm), the O^{18}-incorporated product **2a-O^{18}** (m/z = 198) was also detected (eq. 7, Scheme 3; also see Figure S3, Supporting Information). These results suggest that both water and dioxygen acted as the oxygen source in the formation of pyranone scaffolds. According to reported literatures,[18] the ^{13}C NMR signals of the ^{18}O-attached carbons generally shift to upfield compared to the normal ^{16}O-attached ones. Based on this rule, it has been found that the incorporated ^{18}O in **2a-O^{18}** (both in eq. 6 and eq. 7) predominantly resides in the ester oxygen (δ aryl C-O^{16}: 151.39 ppm; δ aryl C-O^{18}: 151.30 ppm) rather than the carbonyl oxygen (see Figure S2 and S4, Supporting Information). In addition, reaction of **1a** in the presence of both H_2O^{18} and $^{18}O_2$ was also carried out, and the two ^{18}O-incorporated product **2a-(O^{18})$_2$** (m/z = 200) was not detected, suggesting that the original ^{16}O in the formyl group of **1a** can not be substituted by ^{18}O (eq. 8, Scheme 3). Furthermore, an attempt to run the reaction of **1a** under an argon atmosphere was carried out, and the reaction gave **2a** in 36% yield (eq. 9, Scheme 3). In contrast, when **1a** was subjected to the standard reaction conditions except using a dried solvent, the reaction could still give **2a** in 69% yield (eq. 9, Scheme 3). Note that the reaction could also proceed smoothly and give **2a** in 60% yield by using preparative HOCuF[11a] as a catalyst (eq. 10, Scheme 3). Finally, the measurement of the intermolecular KIE on the basis of the competitive C-O coupling between **1a** and **1a-*d*$_5$** was carried out (eq. 11, Scheme 3). The

intermolecular k_H/k_D of **1a** to **1a-d_5** was determined to be 1.42 (Figure S3, see Supporting Information), suggesting that the cleavage of the C-H bond is the rate-determining step.



Scheme 3. Preliminary mechanistic experiments

On the basis of the abovementioned mechanistic studies and previous reports,[11a-c,19] a possible mechanism for the Cu(0)/Selectfluor system-catalyzed double C-H activation/oxygen insertion of 2-phenylbenzaldehydes **1a** was proposed in Scheme 4. Firstly, the redox reaction between the Cu(0) powder and Selectfluor may generate an intermediate F-Cu-BF_4 (**9**) and release a base **10**.[11a-c] Then intermediate **9** may be further converted into XCuOH (**11**, X = F or BF_4) in the aid of base **10** and/or K_2CO_3.[11a-c] Once the active XCuOH species was generated, the reaction may proceed via two possible pathways to form product **2a**. One pathway (path A) might involve an oxycupration of **11** toward the C=O bond in **1a** followed by a fast β-H elimination of the resulting intermediate **12** to give an intermediate **8**. Intermediate **8** may be converted to intermediate **13** in the presence of **11** (also see eq. 5, Scheme 3). Intermediate **13** might undergo intramolecular cross-dehydrogenative C-O coupling reaction[8e,f,12] to afford dibenzopyranone **2a** and regenerate intermediate **11** in the presence of Selecfluor and base (**10** and/or K_2CO_3).[11c] On the other hand, the direct proton abstraction from the formyl group in **1a** by **11** may form an intermediate **14** (path B). The oxidation of **14** with dioxygen followed by a rearrangement of the resulting intermediate **15** would deliver an intermediate **16**,[11a,19] which may be further converted to an intermediate **17**. In presence of Cu(I) species, 17 might decompose to produce an intermediate **18** and hydroxy radical.[12,20] Intermediate **18** may undergo annulation to give an intermediate **19**, which finally delivered the product **2a** after the abstraction of a proton by the hydroxy radical.[12]



Scheme 4. Proposed mechanism

3. Conclusion

In summary, we described an efficient method for the synthesis of dibenzopyranones and pyrazolobenzopyranones directly from 2-arylbenzaldehydes and 5-arylpyrazole-4-carbaldehydes catalyzed by the Cu(0)/Selectfluor system. Preliminary mechanistic studies disclosed that both water and dioxygen acted as the oxygen source in the formation of pyranone scaffolds. The present method for the construction of dibenzopyranones has several advantages including mild reaction conditions, the use of inexpensive copper catalyst, easy availability of the starting materials, and capabilities for the synthesis of heterocyclobenzopyranones.

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 Bruker AVANCE III 500 at 25 °C in $CDCl_3$ at 500 MHz, 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 an Agilent 6890N GC system equipped with a 5973N mass-selective detector with EI source; high resolution mass spectra (HRMS) were obtained on a TOF MS instrument with EI source.

4.2 Typical experimental procedure for the synthesis of the starting materials 2-arybenzaldehydes 1 (or 5-arylpyrazole-4-carbaldehydes 3)

These compounds were synthesized according to the literature procedure.[21] Typical procedure: 2-bromobenzaldehyde (0.92 g, 5 mmol), phenylboronic acid (0.67 g, 5.5 mmol), sodium conbonate (0.53 g, 5 mmol), and $Pd(OAc)_2$ (0.028 g, 0.125 mmol) were added to a flask (50 mL) equipped with a high-vacuum PTFE valve-to-glass seal. The flask was opened to the vacuum, pumped for 2-3 minutes and backfilled with an inert Ar gas. The reaction mixture was stirred at room temperature

overnight. Upon completion, the reaction mixture was diluted with CH_2Cl_2 (3×20 mL) and the organic layer was dried over Na_2SO_4, concentrated under the reduced pressure to give a dark brown oil, which was further purified via column chromatography on Silica gel (eluent: petroleum ether : EtOAc = 20:1) to give 2-phenylbenzaldehyde **1a** (0.86 g, 95%).

4.3 Typical experimental procedure for the synthesis of 2 or 4

1 (or **3**, 0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN (3 mL) were added to a 10-mL flask. Then the reaction mixture was stirred at 25 ºC (50 ºC for **3**) 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** (or **4**).

*4.3.1 6H-benzo[c]chromen-6-one (**2a**).*[22] Prepared from biphenyl-2-carbaldehyde; isolated as white solid (50.6 mg, 86%), m.p. 85–86 °C (lit.[22] m.p. 88–89 °C); IR (KBr, cm^{-1}): ν = 1733, 1602; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (dd, J_1 = 7.5 Hz, J_2 = 1.0Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 8.09 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.87–7.84 (m, 1H), 7.63–7.59 (m, 1H), 7.52–7.49 (m, 1H), 7.41–7.35 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 151.4, 134.8 (2C), 130.6, 130.5, 128.9, 124.6, 122.8, 121.7, 121.4, 118.1, 117.8; GC-MS (EI, 70 eV): m/z (%) = 196 (100) [M^+].

*4.3.2 3-fluoro-6H-benzo[c]chromen-6-one (**2b**).* Prepared from 4'-fluorobiphenyl-2-carbaldehyde; isolated as white solid (52.1 mg, 81%), m.p. 155–157 °C; IR (KBr, cm^{-1}): ν = 1757, 1614; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 8.05–8.02 (m, 2H), 7.85–7.82 (m, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.11–7.07 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (d, J = 250.0 Hz), 160.7, 152.3 (d, J = 12.5 Hz), 135.0, 134.3, 130.7, 128.8, 124.4 (d, J = 10.0 Hz), 121.5, 120.6, 114.7 (d, J = 2.5 Hz), 112.4 (d, J = 22.5 Hz), 105.1 (d, J = 25.0 Hz); HRMS (EI) for $C_{13}H_7FO_2$ [M^+]: calcd. 214.0430, found 214.0427.

*4.3.3 3-chloro-6H-benzo[c]chromen-6-one (**2c**).* Prepared from 4'-chlorobiphenyl-2-carbaldehyde; isolated as white solid (55.3 mg, 80%), m.p. 132–133 °C; IR (KBr, cm^{-1}): ν = 1757, 1606; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (dd, J_1 = 8.0 Hz, J_2 = 1.0Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.88–7.84 (m, 1H), 7.64–7.61 (m, 1H), 7.40 (d, J = 2.0 Hz, 1H), 7.34 (dd, J_1 = 8.5 Hz, J_2 = 2.0Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6, 151.6, 136.0, 135.1, 134.1, 130.8, 129.2, 125.1, 123.8, 121.7, 121.0, 118.0, 116.8; HRMS (EI) for $C_{13}H_7ClO_2$ [M^+]: calcd. 230.0135, found 230.0131.

*4.3.4 3-bromo-6H-benzo[c]chromen-6-one (**2d**).* Prepared from 4'-bromobiphenyl-2-carbaldehyde; isolated as white solid (60.3 mg, 73%), m.p. 140–141 °C; IR (KBr, cm^{-1}): ν = 1752, 1612; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, J = 7.5 Hz, 1H), 8.10 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.56 (d, J = 1.5 Hz, 1H), 7.49(dd, J_1 = 8.0 Hz, J_2 = 1.5Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 151.6, 135.1, 134.1, 130.8, 129.3, 127.9, 124.0, 123.8, 121.7, 121.1, 121.0, 117.2; HRMS (EI) for $C_{13}H_7BrO_2$ [M^+]: calcd. 273.9629, found 273.9635.

*4.3.5 3-(trifluoromethoxy)-6H-benzo[c]chromen-6-one (**2e**).* Prepared from 4'-(trifluoromethoxy)biphenyl-2-carbaldehyde; isolated as white solid (68.9 mg, 82%), m.p. 86–87 °C; IR (KBr, cm^{-1}): ν = 1724, 1609; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 8.06 (dd, J_1 = 8.5 Hz, J_2 = 3.5 Hz, 2H), 7.86–7.83 (m, 1H), 7.62–7.59 (m, 1H), 7.22–7.19 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.4, 151.8, 150.2, 135.1, 133.8, 130.7, 129.3, 124.2, 121.7, 120.9, 120.4 (d, J = 257.5 Hz), 116.9, 116.7, 110.1; HRMS (EI) for $C_{14}H_7F_3O_3$ [M^+]: calcd. 280.0347, found 280.0353.

*4.3.6 3-(tert-butyl)-6H-benzo[c]chromen-6-one (**2f**).* Prepared from 4'-*tert*-butylbiphenyl-2-carbaldehyde; isolated as white solid (40.1 mg, 53%), m.p. 154–156 °C; IR (KBr, cm^{-1}): ν = 1722, 1621; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (dd, J_1 = 8.0 Hz, J_2 = 0.5 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.99 (dd, J_1 = 6.0 Hz, J_2 = 3.0 Hz, 1H), 7.84–7.80 (m, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.40–7.38 (m, 2H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.5, 154.8, 151.3, 135.0, 134.8, 130.6, 128.4, 122.4, 122.0, 121.5, 121.1, 115.4, 114.6, 35.1, 31.1; HRMS (EI) for $C_{17}H_{16}O_2$ [M^+]: calcd. 252.1150, found 252.1146.

*4.3.7 4-chloro-6H-benzo[c]chromen-6-one (**2g**).* Prepared from 3'-chlorobiphenyl-2-carbaldehyde; isolated as white solid (52.6 mg, 76%), m.p. 184–186 °C; IR (KBr, cm^{-1}): ν = 1741, 1605; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.43 (dd, J_1 = 8.0 Hz, J_2 = 1.0Hz, 1H), 8.09 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 2.5 Hz, 1H), 7.89–7.86 (m, 1H), 7.67–7.63 (m, 1H), 7.45 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 7.33 (d, J = 9.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 149.8, 135.0, 133.6, 130.8, 130.3, 130.1, 129.6, 122.6, 121.8, 121.4, 119.4, 119.2; HRMS (EI) for $C_{13}H_7ClO_2$ [M^+]: calcd. 230.0135, found 230.0138.

*4.3.8 9-methyl-6H-benzo[c]chromen-6-one (**2h**).*[23] Prepared from 5-methylbiphenyl-2-carbaldehyde; isolated as white solid (49.2 mg, 78%), m.p. 94–95 °C (lit.[23] m.p. 101–103 °C); IR (KBr, cm^{-1}): ν = 1729, 1615; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, J = 8.0 Hz, 1H), 8.02 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.87 (s, 1H), 7.48–7.45 (m, 1H), 7.38–7.30 (m, 3H), 2.55 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 151.4, 145.9, 134.7, 130.5, 130.2, 130.1, 124.4, 122.7, 121.8, 118.8, 118.1, 117.7, 22.2; GC-MS (EI, 70 eV): *m/z* (%) = 210 (46) [M^+].

*4.3.9 3-fluoro-9-methyl-6H-benzo[c]chromen-6-one (**2i**).* Prepared from 4'-fluoro-5-methylbiphenyl-2-carbaldehyde; isolated as white solid (52.7 mg, 77%), m.p. 152–154 °C; IR (KBr, cm^{-1}): ν = 1730, 1621; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.24 (d, J = 8.5 Hz, 1H), 8.01(dd, J_1 = 9.5 Hz, J_2 = 4.5 Hz, 1H), 7.81 (s, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.08–7.04 (m, 2H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.5 (d, J = 250.0 Hz), 160.8, 152.4 (d, J = 12.5 Hz), 146.2, 134.2, 130.7, 130.0, 124.3 (d, J = 10.0 Hz), 121.7, 118.1, 114.7 (d, J = 2.5 Hz), 112.2 (d, J = 22.5 Hz), 105.1 (d, J = 25.0 Hz), 22.3; HRMS (EI) for $C_{14}H_9FO_2$ [M^+]: calcd. 228.0587, found 228.0584.

*4.3.10 3-chloro-9-methyl-6H-benzo[c]chromen-6-one (**2j**).* Prepared from 4'-chloro-5-methylbiphenyl-2-carbaldehyde; isolated as white solid (52.9 mg, 72%), m.p. 170–171 °C; IR (KBr, cm^{-1}): ν = 1735, 1617; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (d, J = 8.5 Hz, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.83 (s, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 1.0 Hz, 1H), 7.29 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H), 2.56 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.6, 151.7, 146.2, 135.8, 134.0, 130.7, 130.5, 124.9, 123.7, 121.8, 118.5, 117.9, 116.8, 22.3; HRMS (EI) for $C_{14}H_9ClO_2$ [M^+]: calcd. 244.0291, found 244.0295.

*4.3.11 3-bromo-9-methyl-6H-benzo[c]chromen-6-one (**2k**).* Prepared from 4'-bromo-5-methylbiphenyl-2-carbaldehyde; isolated as white solid (60.7 mg, 70%), m.p. 176–178 °C; IR (KBr, cm^{-1}): ν = 1741, 1614; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.28 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.5 Hz, 1H), 7.87 (s, 1H), 7.53 (d, J = 2.0 Hz, 1H), 7.46 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H), 7.42 (d, J = 8.5 Hz, 1H), 2.58 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 151.8, 146.2, 134.1, 130.8, 130.6, 127.7, 123.9,

123.6, 121.8, 121.0, 118.7, 117.3, 22.3; HRMS (EI) for $C_{14}H_9BrO_2$ [M^+]: calcd. 287.9786, found 287.9790.

*4.3.12 3-(tert-butyl)-9-methyl-6H-benzo[c]chromen-6-one (**2l**).* Prepared from 4'-tert-butyl-5-methylbiphenyl-2-carbaldehyde; isolated as white solid (45.5 mg, 57%), m.p. 124–126 °C; IR (KBr, cm^{-1}): ν = 1740, 1611; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.5 Hz, 1H), 7.87 (s, 1H), 7.38–7.36 (m, 3H), 2.56 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.5, 154.6, 151.5, 145.8, 134.9, 130.6, 129.7, 122.3, 121.8, 121.6, 118.7, 115.5, 114.6, 35.0, 31.1, 22.3; HRMS (EI) for $C_{18}H_{18}O_2$ [M^+]: calcd. 266.1307, found 266.1301.

*4.3.13 9-fluoro-6H-benzo[c]chromen-6-one (**2m**).*[5c] Prepared from 5-fluorobiphenyl-2-carbaldehyde; isolated as white solid (41.2 mg, 64%), m.p. 159–161 °C (lit.[5c] m.p. 157–159 °C); IR (KBr, cm^{-1}): ν = 1738, 1604; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (dd, J_1 = 9.0 Hz, J_2 = 5.5 Hz, 1H), 7.97 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.75 (dd, J_1 = 9.5 Hz, J_2 = 2.0 Hz, 1H), 7.56–7.52 (m, 1H), 7.40–7.35 (m, 2H),7.30–7.27 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 167.0 (d, J = 255.0 Hz), 160.2, 151.7, 137.8 (d, J = 10.0 Hz), 134.0 (d, J = 10.0 Hz), 131.3, 124.7, 123.0, 118.0, 117.9 (d, J = 1.3 Hz), 117.4 (d, J = 2.5 Hz), 117.0 (d, J = 22.5 Hz), 108.2 (d, J = 22.5 Hz); GC-MS (EI, 70 eV): *m/z* (%) = 214 (100) [M^+].

*4.3.14 9-chloro-6H-benzo[c]chromen-6-one (**2n**).*[5c] Prepared from 5-chlorobiphenyl-2-carbaldehyde; isolated as white solid (52.6 mg, 76%), m.p. 172–174 °C (lit.[5c] m.p. 182–184 °C); IR (KBr, cm^{-1}): ν = 1735, 1602; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, J = 8.5 Hz, 1H), 8.08 (d, J = 2.0 Hz, 1H), 8.01 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.55–7.51 (m, 2H), 7.39–7.35 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.3, 151.7, 141.9, 136.4, 132.3, 131.2, 129.3, 124.8, 122.9, 121.8, 119.7, 118.0, 117.1; GC-MS (EI, 70 eV): *m/z* (%) = 230 (100) [M^+].

*4.3.15 8-fluoro-6H-benzo[c]chromen-6-one (**2o**).* Prepared from 4-fluorobiphenyl-2-carbaldehyde; isolated as white solid (46.9 mg, 73%), m.p. 139–141 °C; IR (KBr, cm^{-1}): ν = 1717, 1608; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (dd, J_1 = 9.0 Hz, J_2 = 5.0 Hz, 1H), 8.05 (d, J = 3.0 Hz, 1H), 8.00 (dd, J_1 = 7.5 Hz, J_2 = 1.0 Hz, 1H),7.57–7.53 (m, 1H), 7.37 (d, J = 2.0 Hz, 1H), 7.33 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.5 (d, J = 248.8 Hz), 160.1 (d, J = 2.5 Hz), 150.9, 131.3 (d, J = 2.5 Hz), 130.4, 124.8, 124.3 (d, J = 7.5 Hz), 123.2 (d, J = 8.8 Hz), 123.0 (d, J = 22.5 Hz), 122.6, 117.9, 117.4, 116.2 (d, J = 22.5 Hz); HRMS (EI) for $C_{13}H_7FO_2$ [M^+]: calcd. 214.0430, found 214.0428.

*4.3.16 3-chloro-8-fluoro-6H-benzo[c]chromen-6-one (**2p**).* Prepared from 4'-chloro-4-fluorobiphenyl-2-carbaldehyde; isolated as white solid (46.2 mg, 62%), m.p. 192–193 °C; IR (KBr, cm^{-1}): ν = 1733, 1607; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.08 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 8.03 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.59–7.55 (m, 1H), 7.37 (d, J = 2.0 Hz, 1H), 7.33 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 162.7 (d, J = 250.0 Hz), 159.5 (d, J = 3.8 Hz), 151.1, 136.0, 130.6 (d, J = 3.8 Hz), 125.3, 124.3 (d, J = 7.5 Hz), 123.6, 123.3 (d, J = 23.8 Hz), 122.9 (d, J = 7.5 Hz), 118.1, 116.4 (d, J = 23.8 Hz), 116.1; HRMS (EI) for $C_{13}H_6ClFO_2$ [M^+]: calcd. 248.0040, found 248.0045.

*4.3.17 8-chloro-6H-benzo[c]chromen-6-one (**2q**).* Prepared from 4-chlorobiphenyl-2-carbaldehyde; isolated as white solid (49.8 mg, 72%), m.p. 171–172 °C; IR (KBr, cm^{-1}): ν = 1720, 1601; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (d, J = 2.0 Hz, 1H), 8.08 (d, J = 8.5 Hz, 1H), 8.03 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.79 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H), 7.54–7.50 (m, 1H), 7.40–7.36 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.0, 151.2, 135.2, 135.1, 133.3, 130.9, 130.1, 124.8, 123.4, 122.8, 122.7, 117.9, 117.4; HRMS (EI) for $C_{13}H_7ClO_2$ [M^+]: calcd. 230.0135, found 230.0138.

*4.3.18 8-chloro-3-fluoro-6H-benzo[c]chromen-6-one (**2r**).* Prepared from 4-chloro-4'-fluorobiphenyl-2-carbaldehyde; isolated as white solid (60.4 mg, 81%), m.p. 208–210 °C; IR (KBr, cm^{-1}): ν = 1746, 1608; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.37 (d, J = 2.0 Hz, 1H), 8.03–8.00 (m, 2H), 7.79 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H), 7.14–7.10 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7 (d, J = 250.0 Hz), 159.7, 152.1 (d, J = 12.5 Hz), 135.4, 135.0, 132.8, 130.2, 124.4 (d, J = 10.0 Hz), 123.3, 121.9, 114.0 (d, J = 3.8 Hz), 112.8 (d, J = 22.5 Hz), 105.4 (d, J = 25.0 Hz); HRMS (EI) for $C_{13}H_6ClFO_2$ [M^+]: calcd. 248.0040, found 248.0037.

*4.3.19 8-bromo -6H-benzo[c]chromen-6-one (**2s**).* Prepared from 4-bromobiphenyl-2-carbaldehyde; isolated as white solid (58.6 mg, 71%), m.p. 162–164 °C; IR (KBr, cm^{-1}): ν = 1735, 1598; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.56 (d, J = 2.0 Hz, 1H), 8.05 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.94 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 7.82–7.78 (m, 1H), 7.55–7.52 (m, 1H), 7.41–7.36 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.9, 151.2, 138.0, 133.7, 133.2, 130.9, 124.9, 123.5, 122.81, 122.78, 122.75, 118.0, 117.4; HRMS (EI) for $C_{13}H_7BrO_2$ [M^+]: calcd. 273.9629, found 273.9626.

*4.3.20 8-methoxy -6H-benzo[c]chromen-6-one (**2t**).*[8f] Prepared from 4-methoxybiphenyl-2-carbaldehyde; isolated as white solid (21.0 mg, 31%), m.p. 153–155 °C (lit.[8f] m.p. 149–151 °C); IR (KBr, cm^{-1}): ν = 1710, 1613; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (d, J = 9.0 Hz, 1H), 8.01 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 7.84 (d, J = 2.5 Hz, 1H), 7.47–7.41 (m, 2H), 7.38 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 7.36–7.33 (m, 1H), 3.96 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 160.2, 150.6, 129.4, 128.2, 124.6, 124.3, 123.5, 122.6, 122.2, 118.3, 117.7, 111.4, 55.8; GC-MS (EI, 70 eV): *m/z* (%) = 226 (38) [M^+].

*4.3.21 8-methoxy-3-(trifluoromethoxy)-6H-benzo[c]chromen-6-one (**2u**).* Prepared from 4-methoxy-4'-(trifluoromethoxy)biphenyl-2-carbaldehyde; isolated as white solid (46.5 mg, 50%), m.p. 90–92 °C; IR (KBr, cm^{-1}): ν = 1733, 1615; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, J_1 = 8.5 Hz, J_2 = 5.0 Hz, 2H), 7.74 (d, J = 3.0 Hz, 1H), 7.38 (dd, J_1 = 9.0 Hz, J_2 = 3.0 Hz, 1H), 7.18–7.16 (m, 2H), 3.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.5, 160.3, 150.7, 149.2, 127.0, 124.4, 123.42, 123.39, 122.0, 120.4(d, J = 256.3 Hz), 117.0, 116.9, 111.4, 110.0, 55.8; HRMS (EI) for $C_{15}H_9F_3O_4$ [M^+]: calcd. 310.0453, found 310.0457.

*4.3.22 7-fluoro -6H-benzo[c]chromen-6-one (**2v**).* Prepared from 3-fluorobiphenyl-2-carbaldehyde; isolated as white solid (55.9 mg, 87%), m.p. 149–151 °C; IR (KBr, cm^{-1}): ν = 1729, 1606; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.82–7.78 (m, 1H), 7.52–7.49 (m, 1H), 7.36–7.33 (m, 2H), 7.28–7.25 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.6 (d, J = 266.3 Hz), 156.7 (d, J = 5.0 Hz), 151.6, 137.4, 136.2 (d, J = 11.3 Hz), 131.2, 124.7, 123.3, 117.7, 117.6 (d, J = 5.0 Hz), 117.1 (d, J = 2.5 Hz), 116.4 (d, J = 22.5 Hz), 110.2 (d, J = 6.3 Hz); HRMS (EI) for $C_{13}H_7FO_2$ [M^+]: calcd. 214.0430, found 214.0435.

*4.3.23 3-methyl-1-phenylchromeno[4,3-c]pyrazol-4(1H)-one (**4a**).*[24] Prepared from 3-methyl-1,5-diphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (55.5 mg, 67%), m.p. 222–224 °C (lit.[24] 226–227 °C); IR (KBr, cm^{-1}): ν = 1729, 1621; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64–7.60 (m, 3H), 7.58–7.54 (m, 2H), 7.46–7.39 (m, 2H), 7.11 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.06–7.01 (m, 1H), 2.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ

158.0, 153.3, 150.8, 141.7, 139.4, 131.1, 130.2, 129.9, 126.9, 123.9, 122.5, 118.1, 111.9, 106.4, 12.9; GC-MS (EI, 70 eV): *m/z* (%) = 276 (22) [M^+].

*4.3.24 7-fluoro-3-methyl-1-phenylchromeno[4,3-c]pyrazol-4(1H)-one (**4b**).* Prepared from 5-(4-fluorophenyl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (61.8 mg, 70%), m.p. 224–226 °C; IR (KBr, cm^{-1}): ν = 1743, 1624; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65–7.61 (m, 3H), 7.57–7.53 (m, 2H), 7.13 (dd, J_1 = 9.0 Hz, J_2 = 2.5 Hz, 1H), 7.09 (dd, J_1 = 9.0 Hz, J_2 = 5.5 Hz, 1H), 6.81–6.76 (m, 1H), 2.67 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.7(d, J = 251.3 Hz), 157.5, 154.6 (d, J = 12.5 Hz), 150.9, 141.2, 139.2, 130.3, 130.0, 126.9, 124.0 (d, J = 12.5 Hz), 111.8 (d, J = 22.5 Hz), 108.6 (d, J = 2.5 Hz), 105.5 (d, J = 21.3 Hz), 105.4; HRMS (EI) for $C_{17}H_{11}FN_2O_2$ [M^+]: calcd. 294.0805, found 294.0808.

*4.3.25 7-chloro-3-methyl-1-phenylchromeno[4,3-c]pyrazol-4(1H)-one (**4c**).* Prepared from 5-(4-chlorophenyl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (67.1 mg, 72%), m.p. 170–172 °C; IR (KBr, cm^{-1}): ν = 1745, 1621; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64–7.61(m, 3H), 7.55–7.53 (m, 2H), 7.38 (s, 1H), 7.01 (d, J = 2.0 Hz, 2H), 2.66 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.2, 153.5, 150.9, 140.9, 139.1, 136.8, 130.3, 123.0, 126.8, 124.4, 123.2, 118.2, 110.4, 106.0, 12.8; HRMS (EI) for $C_{17}H_{11}ClN_2O_2$ [M^+]: calcd. 310.0509, found 310.0505.

*4.3.26 7-(tert-butyl)-3-methyl-1-phenylchromeno[4,3-c]pyrazol-4(1H)-one (**4d**).* Prepared from 5-(4-*tert*-butylphenyl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (54.8 mg, 55%), m.p. 210–212 °C; IR (KBr, cm^{-1}): ν = 1734, 1622; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62–7.58 (m, 3H), 7.57–7.53 (m, 2H), 7.44 (d, J = 2.0 Hz, 1H), 7.09 (dd, J_1 =8.5 Hz, J_2 = 1.5 Hz, 1H), 7.04 (d, J = 8.5 Hz, 1H), 2.67 (s, 3H), 1.30 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.2, 155.4, 153.4, 150.7, 141.9, 139.4, 130.0, 129.8, 126.8, 122.0, 121.4, 114.7, 109.1, 106.0, 35.1, 30.9, 12.8; HRMS (EI) for $C_{21}H_{20}N_2O_2$ [M^+]: calcd. 332.1525, found 332.1529.

*4.3.27 9-chloro-3-methyl-1-phenylchromeno[4,3-c]pyrazol-4(1H)-one (**4e**).* Prepared from 5-(2-chlorophenyl)-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (55.9 mg, 60%), m.p. 108–110 °C; IR (KBr, cm^{-1}): ν = 1795, 1676; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (dd, J_1 = 8.0 Hz, J_2 = 0.5 Hz, 1H), 7.41–7.36 (m, 1H), 7.32–7.29 (m, 3H), 7.27–7.23 (m, 3H), 2.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.6, 153.6, 152.0, 145.7, 138.5, 134.2, 131.6, 131.3, 129.8, 129.0, 128.5, 128.3, 126.8, 124.7, 108.2, 107.7, 13.9; HRMS (EI) for $C_{17}H_{11}ClN_2O_2$ [M^+]: calcd. 310.0509, found 310.0512.

*4.3.28 1,3-diphenylchromeno[4,3-c]pyrazol-4(1H)-one (**4f**) and 2,3-diphenylchromeno[4,3-c] pyrazol -4(2H)-one (**4f'**) (**4f**:**4f'** = 1:0.41).* Prepared from 1,3,5-triphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (62.9 mg, 62%); IR (KBr, cm^{-1}): ν = 1736, 1609; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23–8.20 (m, 2H, **4f**), 7.69–7.63 (m, 3.64H, 2H for **4f**; 1.64H for **4f'**), 7.54–7.34 (m, 12.69H, 9H for **4f**, 3.69H for **4f'**), 7.11–7.04 (m, 1.41H, 1H for **4f**, 0.41H for **4f'**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.8, 157.3, 153.2, 153.1, 152.6, 149.2, 146.2, 142.8, 139.6, 139.1, 131.2, 130.60, 130.57, 130.5, 130.4, 130.01, 129.95, 129.4, 129.24, 129.17, 128.9, 128.4, 128.3, 127.1, 127.0, 125.9, 124.4, 123.9, 122.8, 122.5, 117.9, 117.4, 114.8, 111.6, 106.1, 104.9; HRMS (EI) for $C_{22}H_{14}N_2O_2$ [M^+]: calcd. 338.1055, found 338.1051.

*4.3.29 7-chloro-1,3-diphenylchromeno[4,3-c]pyrazol-4(1H)-one (**4g**).* Prepared from 5-(4-chlorophenyl)-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (73.8 mg, 66%), m.p. 195–197 °C; IR (KBr, cm^{-1}): ν = 1735, 1609; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.54–7.51 (m, 1H), 7.45–7.41 (m, 4H), 7.39–7.34 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.8, 153.0, 149.4, 144.9, 138.9, 136.3, 131.9, 130.7, 129.4, 129.1, 128.8, 125.9, 125.4, 124.5, 122.9, 117.5, 114.7, 106.2; HRMS (EI) for $C_{22}H_{13}ClN_2O_2$ [M^+]: calcd. 372.0666, found 372.0661.

*4.3.30 7-bromo-1,3-diphenylchromeno[4,3-c]pyrazol-4(1H)-one (**4h**).* Prepared from 5-(4-bromophenyl)-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (78.9 mg, 63%), m.p. 200–202 °C; IR (KBr, cm^{-1}): ν = 1739, 1590; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.55–7.51 (m, 3H), 7.45–7.41 (m, 4H), 7.38–7.31 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.8, 153.0, 149.4, 144.9, 138.8, 132.0, 131.8, 130.7, 129.4, 129.1, 125.9, 125.9, 124.7, 124.5, 122.9, 117.5, 114.6, 106.2; HRMS (EI) for $C_{22}H_{113}BrN_2O_2$ [M^+]: calcd. 416.0160, found 416.0155.

*4.3.31 9-chloro-1,3-diphenylchromeno[4,3-c]pyrazol-4(1H)-one (**4i**).* Prepared from 5-(2-chlorophenyl)-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (55.9 mg, 50%), m.p. 172–173 °C; IR (KBr, cm^{-1}): ν = 1746, 1610; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (dd, J_1 = 7.5 Hz, J_2 = 1.5Hz, 1H,),7.53–7.50 (m, 1H), 7.48–7.44 (m, 1H),7.43–7.34 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.2, 153.1, 149.1, 142.9, 138.9, 134.21, 132.1, 131.5, 130.6, 130.0, 129.1, 128.8, 127.2, 126.9, 124.8, 124.4, 122.8, 117.5, 114.7, 107.8; HRMS (EI) for $C_{22}H_{13}ClN_2O_2$ [M^+]: calcd. 372.0666, found 372.0669.

*4.3.32 9-bromo-1,3-diphenylchromeno[4,3-c]pyrazol-4(1H)-one (**4j**).* Prepared from 5-(2-bromophenyl)-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as brown solid (56.3 mg, 45%), m.p. 198–199 °C; IR (KBr, cm^{-1}): ν = 1735, 1609; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H,), 7.66 (d, J = 8.0 Hz,1H), 7.54–7.50 (m, 1H), 7.43–7.34 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.2, 153.1, 149.0, 144.4, 138.9, 133.2, 132.1, 131.6, 130.6, 129.4, 129.1, 128.8, 127.5, 125.0, 124.5, 124.0, 122.9, 117.6, 114.8, 107.8; HRMS (EI) for $C_{22}H_{13}BrN_2O_2$ [M^+]: calcd. 416.0160, found 416.0167.

*4.3.33 3-(4'-bromophenyl)-7-chloro-2-phenylchromeno[4,3-c]pyrazol-4(2H)-one (**4k**) and 7-bromo -3-(4'-chlorophenyl)-1-phenylchromeno[4,3-c]pyrazol-4(1H)-one (**4k'**) (**4k**:**4k'** = 1:0.94).* Prepared from 5-(4-bromophenyl)-1,3-diphenyl-1*H*-pyrazole-4-carbaldehyde; isolated as Brown solid (85.4 mg, 63%); IR (KBr, cm^{-1}): ν = 1743, 1612; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, J = 8.5 Hz, 2H, **4k**), 8.11 (d, J = 8.5 Hz, 0.94H, **4k'**), 7.69–7.60 (m, 6H, **4k**), 7.53 (d, J = 8.5 Hz, 1.88H, **4k'**), 7.48–7.42 (m, 5.82H, 3H for **4k**, 2.82H for **4k'**), 7.36–7.30 (m, 4.76H, 1H for **4k**, 3.76H for **4k'**), 7.19 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 0.94H, **4k'**), 6.92 (d, J = 8.5 Hz, 0.94H, **4k'**); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.1, 156.6, 153.3, 153.2, 151.6, 148.6, 145.1, 142.3, 139.2, 138.7, 136.2, 135.7, 132.0, 131.8, 130.8, 130.5, 130.2, 129.5, 129.2, 128.9, 128.6, 127.4, 127.0, 125.8, 125.6, 125.1, 125.0, 124.9, 123.8, 123.4, 121.1, 117.8, 113.3, 110.4, 105.8, 104.7; HRMS (EI) for $C_{22}H_{12}BrClN_2O_2$ [M^+]: calcd. 449.9771, found 449.9775.

4.4 Synthesis of 2'-hydroxy-(1,1'-biphenyl)-2-carboxylic acid 5

2a (58.8 mg, 0.3 mmol) and MeCN (3 mL) was added to a flask (10 mL), then NaOH aqueous solution (5% (W/W), 2 mL) was dropped. After stired for 3 h at room temperature, the reaction mixture was wished with CH_2Cl_2 (3×5 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 (10/1, V/V) as eluent to give pure **5**.

4.4.1 2'-hydroxy-(1,1'-biphenyl)-2-carboxylic acid (5).[25] Prepared from 6*H*-benzo[*c*]chromen-6-one; isolated as white solid (63.0 mg, 98%), m.p. 90–91 °C (lit.[25] 93 °C); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, J = 7.5 Hz, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 7.5 Hz, 1H), 7.60 (t, J = 7.0 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.39–7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.2, 151.3, 134.82, 134.77, 130.6, 130.4, 128.9, 124.5, 122.8, 121.7, 121.3, 118.1, 117.8.

4.5 Synthesis of 6*H*-benzo[*c*]chromen 6

2a (58.8 mg, 0.3 mmol), $NaBH_4$ (17.1 mg, 0.45 mmol) and EtOH (3 mL) was added to a flask (10 mL) and stired for 6 h at room temperature. The reaction mixture was wished with CH_2Cl_2 (3×5 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 (10/1, V/V) as eluent to give pure **6**.

4.5.1 6H-benzo[c]chromen (6). Prepared from 6*H*-benzo[*c*]chromen-6-one; isolated as white solid (50.3 mg, 92%), m.p. 130–132 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52–7.50 (m, 1H), 7.42–7.40 (m, 2H), 7.29–7.26 (m, 2H), 7.12 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 7.02–6.99 (m, 1H), 6.95 (d, J = 8.5 Hz, 1H), 4.48–4.42 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.9, 138.9, 136.5, 130.9, 130.8, 129.4, 129.3, 128.6, 128.5, 127.8, 120.8, 116.4, 63.7.

4.6 Synthesis of 6-phenyl-6*H*-benzo[*c*]chromen-6-ol 7

Under an atmosphere of Ar gas, **2a** (58.8 mg, 0.3 mmol) and THF (3 mL) was added to a flask (10 mL), then PhMgBr (0.4 mL) was dropped. After stired for 3 h at room temperature, the reaction mixture was quenched with saturated ammonium chloride solution and diluted with CH_2Cl_2 (3×5 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 (6/1, V/V) as eluent to give pure **7**.

4.6.1 6-phenyl-6H-benzo[c]chromen-6-ol (7). Prepared from 6*H*-benzo[*c*]chromen-6-one; isolated as white solid (77.4 mg, 94%), m.p. 81–83 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01–7.98 (m, 2H), 7.63 (s, 1H), 7.55–7.52 (m, 2H), 7.48–7.44 (m, 1H), 7.42–7.37 (m, 3H), 7.32–7.27 (m, 2H), 7.12–7.09 (m, 1H), 7.04 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 6.92 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 151.3, 143.0, 135.4, 129.4, 128.7, 128.5, 128.1, 127.7, 127.5, 126.8, 126.3, 123.1, 123.0, 121.7, 121.1, 117.8, 99.2.

4.7 Mechanistic Studies

4.7.1 Preparation of (1,1'-biphenyl)-2-carboxylic acid 8

8 was synthesized according to reported literature.[8k] Procedure: To a solution of phenylboronic acid (2.1 mmol) in dry THF (4.5 mL) was added a prepared suspension of $PdCl_2(PPh_3)_2$ in dry THF (0.5 mL, 0.1 M). The suspension was stirred and a Na_2CO_3 aqueous solution (5 mL, 0.8 M) was added. The reaction mixture was stirred under Ar atmosphere for 2 min. at room temperature. Finally, methyl 2-iodobenzoate (294 µL, 2 mmol) was added and the reaction mixture was heated at 80 °C for 12 h under Ar atmosphere. The resultant mixture was extracted with EtOAc (3×10 mL). The combined layers were washed with brine (1×5 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/EtOAc = 95:5 (V/V) to provide the corresponding methyl esters as pale yellow oils.

A NaOH aqueous solution (7 mL, 1 M) was added to a stirring mixture of the desired ester (1.8 mmol) in MeOH (7 mL) under Ar atmosphere. The reaction mixture was heated to 50 °C for 12 h. Upon completion, the reaction mixture was concentrated under reduced pressure. The residue was quenched with 6 M HCl until pH < 3 and was extracted with EtOAc (3×10 mL). The combined layers were washed with brine (1×5 mL), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to afford the desired pure biaryl 2-carboxylic acids **8**

4.7.1.1 (1,1'-biphenyl)-2-carboxylic acid (8). Prepared from methyl biphenyl-2-carboxylate6; isolated as Pink solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.39 (s, 1H), 7.97 (d, J = 7.5 Hz, 1H), 7.61–7.57 (m, 2H), 7.36–7.36 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 173.4, 143.4, 141.0, 132.1, 131.2, 130.7, 129.3, 128.5, 128.1, 127.4, 127.2.

4.7.2 Subjection of 8 to the standard reaction conditions

8 (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN (3 mL) were added to a 10-mL flask. Then the reaction mixture was stirred at 25 °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 **2a** (55.9 mg, 95%).

4.7.3 Reaction of 1a in CH_3CN-H_2O^{18} (200:1, V/V)

1a (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN:H_2O^{18} = 200:1 (V/V, 3 mL) were added to a 10-mL flask. Then the reaction mixture was stirred at 25 °C for 24 h. Upon completion, the resulting mixture was sampled for GC-MS analysis (see Figure S1).

4.7.4 Reaction of 1a under the standard reaction conditions except in the presence of $^{18}O_2$ atmosphere

1a (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN:H_2O = 200:1 (V/V, 3 mL) were added to a 10-mL flask. The flask was opened to the vacuum, pumped for 2-3 minutes and backfilled with $^{18}O_2$ gas using a balloon. Then the reaction mixture was stirred at 25 °C for 24 h. Upon completion, the resulting mixture was sampled for GC-MS analysis (see Figure S2).

4.7.5 Reaction of 1a under the standard reaction conditions except in the presence of $^{18}O_2$ atmosphere and H_2O^{18}

1a (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN:H_2O^{18} = 200:1 (V/V, 3 mL) were added to a 10-mL flask. The flask was opened to the vacuum, pumped for 2-3 minutes and backfilled with $^{18}O_2$ gas using a balloon. Then the reaction mixture was stirred at 25 °C for 24 h. Upon completion, the resulting mixture was sampled for GC-MS analysis. It has been found that the two ^{18}O-incorporated product **2a-(O^{18})$_2$** (m/z = 200) was not detected.

4.7.6 Reaction of 1a under the standard reaction conditions except under an argon atmosphere

1a (0.3 mmol), Cu(0) powder (1.92 mg, 10 mol %), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN:H_2O = 200:1 (V/V, 3 mL) were added to a 10-mL flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the resultant mixture in the sealed tube was frozen by immersion of the flask in liquid N_2. When solvent was completely frozen, the flask was opened to the vacuum (high vacuum) and pumped for 2-3 minutes, with the flask still immersed in liquid N_2. The flask was then closed and warmed until solvent completely melted. This process was repeated three times and after the last cycle the flask was backfilled with an inert Ar gas. Then the reaction mixture was stirred at 25 ºC 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 **2a** (21.2 mg, 36%).

4.7.7 Reaction of 1a under the standard reaction conditions except using dried CH_3CN

The procedure is similar to the one described in 4.3 except using a dried CH_3CN. The reaction gave pure **2a** in 69% yield (40.6 mg).

4.7.8 Reaction of 1a under the standard reaction conditions except using HOCuF as a catalyst

1a (0.3 mmol), HOCuF (10 mol %, prepared according to our previous work[11a]), Selectfluor (212.6 mg, 0.6 mmol), K_2CO_3 (82.8 mg, 0.6 mmol) and CH_3CN:H_2O = 200:1 (V/V, 3 mL) were added to a 10-mL flask. Then the reaction mixture was stirred at 25 ºC 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 **2a** (35.3 mg, 60%).

4.7.9 Determination of intermolecular kinetic isotope effect of 1a and 1a-d_5

To a 25-mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal was sequentially added **1a**-d_5 (37.4 mg, 0.2 mmol), **1a** (36.4 mg, 0.2 mmol), Cu(0) powder (2.56 mg, 10 mol %), Selectfluor (283.5 mg, 0.8 mmol, 2 equiv), and CH_3CN (3.5 mL) were added to a 10-mL flask. Then the reaction mixture was stirred at 25 ºC for 6 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 (10/1, V/V) as eluent to give the mixture of **2a** and **2a**-d_4. Based on the ^{1}H NMR spectral analyses, the kinetic isotope effect is calculated to be $k_H/k_D = 1.42 \pm 0.2$ (see Figure S3).

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Supplementary data (charts for mechanistic studies as well as copies of ^{1}H & ^{13}C NMR spectra of the compounds) associated with this article can be found in the online version, at http://.

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