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Synthesis of Biheterocycles Based on Quinolinone, Chromone, and Coumarin Scaffolds by Palladium-Catalyzed Decarboxylative Couplings

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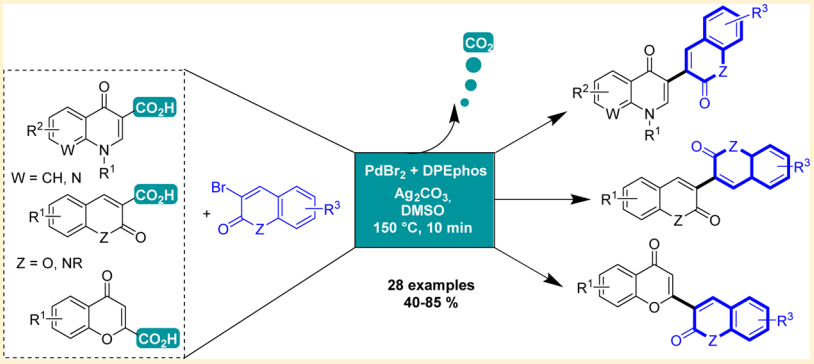
Supporting Information



ABSTRACT: An efficient Pd-catalyzed decarboxylative coupling of heterocyclic carboxylic acids with heterocyclic halides to achieve the synthesis of biheterocycles of biological interest has been reported. In all cases, the cross-coupling reactions take place rapidly in DMSO in good yields and efficiently proceed in the presence of a $PdBr_2$/DPEphos catalytic system, furnishing the novel biheterocycles based on quinolin-4-one, quinolin-2-one, chromone, and coumarin scaffolds.

1. INTRODUCTION

Biheterocycles represent an important class of organic derivatives, which have attracted considerable attention due to their widespread application in organic synthesis, advanced materials, and pharmaceuticals.[1] On one hand, quinolinone-containing biheterocycles are an important constituent of various biologically active compounds, including topoisomerase inhibitors,[2] adenosine A2B antagonists,[3] and multikinase inhibitors[4] (Figure 1). On the other hand, the quinolin-2(1*H*)-one[5] and coumarin[6] frameworks as well as chromone units[7] are present in a very broad range of natural and non-natural products of biological interest. Over the past decades, synthesis and screening of these heterocyclic compounds for drug discovery has been a subject of constant interest in medicinal chemistry. Derivatization of these heterocyclic pharmacophores represents a convenient approach to generate chemical diversity during lead identification and optimization. Thus, the combination of these privileged structures in single chemical entities, as depicted in Figure 1, may lead to the identification of novel "multifunctional ligands" able to interfere with different biological pathways in a dual way.

Traditional strategies for the preparation of such molecules employ the coupling of a heterocyclic halide with an organometallic heterocyclic derivative under palladium catalysis. However, this strategy requires the preparation and use of stoichiometric amounts of organometallic derivatives such as $HetArB(OR)_2$, HetArZnX, HetArMgX, or $HetArSnR_3$, in which instability of the C−M bond, in some cases, lessens their synthetic utility.

As part of our continuing efforts at the functionalization of heterocycles via transition metal-catalyzed reactions,[8] combined with our interest in discovering novel scaffolds of biological interest, we required the synthesis of biheterocycles based on quinolin-2-one, quinolin-4-one coumarin, or chromone scaffolds (Figure 1). Their preparation was envisioned through a palladium-catalyzed decarboxylative coupling of a heterocyclic carboxylic acid with another heterocyclic halide. This procedure, which generated minimum waste upon decarboxylation, places this transformation among the greenest alternatives to traditional cross-couplings.[9] Despite the great success of this reaction in the formation of *heteroarene−aryl* units via the coupling of heteroarene carboxylic acids with aryl halides,[10] similar strategies for the construction of *heterocycle−heterocycle* units such as quinolinone−coumarin remain far less explored. In this area, very recently, we have reported a highly efficient and versatile decarboxylative coupling reaction of quinolinone-3-carboxylic acids[8e] with (hetero)aryl halides. The bimetallic system composed of $PdBr_2$/DPEphos/Ag_2CO_3 enables high-yielding reactions with various (hetero)aryl

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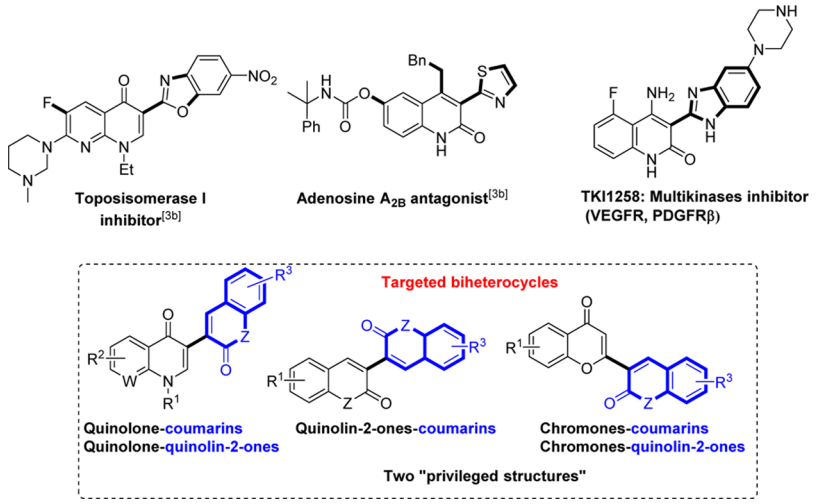

Figure 1. Chemical structures of bioactive biheterocycles and targeted products.

halides. In addition, we demonstrated through a preliminary result that the use of these conditions also enabled, for the first time, decarboxylative coupling of quinolinone-3-carboxylic acid **1a** with 3-bromocoumarin or quinolin-2(1*H*)-one to provide **3a** and **4a** in moderate yields (40% and 56%, respectively, Scheme 1).

Scheme 1. Pd-Catalyzed Decarboxylative Coupling of 1a with 3-Bromocoumarin and Quinolinone under our Previously Optimized Conditions

Given the practical importance of efficient *biheterocycle* syntheses for the purpose of our medicinal chemistry program, we were interested in extending the scope of the palladium-catalyzed decarboxylative coupling of quinolin-4-one-3-carboxylic acids with various coumarins and quinolin-2-ones. In these cases, all our attempts to increase the yields of **3a** and **4a** by using high catalyst loading (up to 20 mol %) and elevated temperatures (up to 170 °C) combined with a prolonged reaction time did not lead to any improvement. These unsuccessful results clearly demonstrate that the nature of the heterocyclic substrates play a critical role in the outcome of this decarboxylative coupling reaction. To address difficulties associated with the reactivity of coumarin and quinolin-2(1*H*)-one derivatives, we decided to investigate these challenging couplings by fine-tuning of the reaction conditions. The results of this study are now reported.

2. RESULTS AND DISCUSSION

Initial investigations were performed coupling quinolin-4-one 3-carboxylic acid **1a** with 3-bromocoumarin **2a** as a model study (Table 1). When the reaction was performed using our previously reported procedure [$PdBr_2$ (5 mol %), DPEphos (10 mol %); Ag_2CO_3 (1 equiv) in toluene:DMA at 150 °C for 1 h under microwave irradiation], only 40% yield of **3a** was obtained (Table 1, entry 1). A similar yield was obtained when the reaction was heated in an oil bath at 150 °C for 3 h in a mixture toluene/DMA 1:1 (entry 2) or in DMSO (entry 3).

Interestingly, increasing the amount of the phosphine (up to 20 mol %) in otherwise the same conditions drives the coupling to completion, and 3-coumarino-3-ylquinolinone **3a** was obtained in a 60% yield (entry 4). This result is consistent with the possibility of the phosphine ligand to act as a reducing agent to convert Pd to Pd(0). Moreover, decreasing the reaction time into 30 min led to a similar yield (entry 5), whereas the yield of **3a** increases to 76% when the reaction was run for only 10 min (entry 6). It should be noted that the palladium catalyst is necessary to achieve this transformation because no reaction occurs when the coupling is conducted in the absence of $PdBr_2$. A brief survey of palladium catalysts revealed that the source of the catalyst has an influence in the outcome of the reaction. We were delighted to find that the use of $PdBr_2$ in combination with DPEphos for only 10 min heating at 150 °C is the best combination of the coupling reaction with yield of **3a** up to 76% (entry 6). A similar yield was obtained when the reaction of **1a** and **2a** was performed with $Pd(OAc)_2$ (entry 9), whereas $PdCl_2$, PdI_2, and $Pd(acac)_2$ were less efficient (entries 7, 8, and 10). The screening of other solvents revealed that DMSO is the most effective (entries 6, 11, and 12). In summary, the best conditions were found to require **1a** (1 equiv), **2a** (2 equiv), $PdBr_2$ (5 mol %), DPEphos (20 mol %), Ag_2CO_3 (1 equiv), and DMSO in a sealed tube at 150 °C for 10 min (entry 6). It should be noted that this coupling of **1a** with **2a** is not limited to a small scale (0.56 mmol), as it could be conveniently performed on a gram-scale (2 mmol, 4-fold scale up) in a slightly lower yield.

With a viable coupling procedure in hand, attention was turned to the generality of the process, and the couplings of structurally diverse heterocyclic carboxylic acids with diverse heterocyclic halides. Remarkably, this heterocycle−heterocycle coupling reaction appeared to be quite general with respect to both heterocyclic partners (Tables 2 and 3), and in all cases no homocoupled byproducts were detected. First, we investigated the scope of the Pd-catalyzed decarboxylative coupling of various substituted quinolin-4-ones 3-carboxylic acids **1** with 3-bromocoumarins and 3-bromoquinolin-2-ones **2** possessing different steric and electronic properties. Gratifyingly, all the couplings proceeded cleanly and selectively in good to excellent

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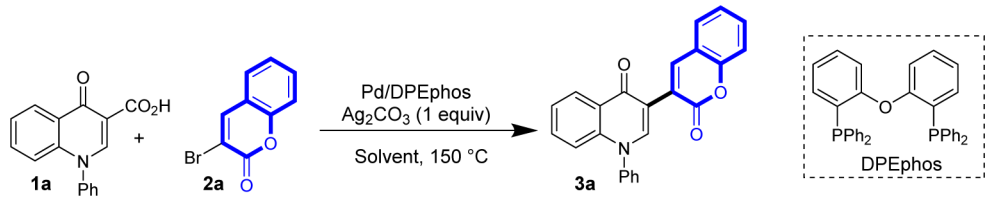
Table 1. Optimization of the Coupling Reaction of 1a with 3-Bromocoumarin 2a[a]



entry	[Pd]	ligand	solvent	time (min)	yield[b] (%)
1	$PdBr_2$	DPEphos[c]	PhMe:DMA	60	40
2	$PdBr_2$	DPEphos[c]	PhMe:DMA	180	41
3	$PdBr_2$	DPEphos[c]	DMSO	60	40
4	$PdBr_2$	DPEphos	DMSO	60	60
5	$PdBr_2$	DPEphos	DMSO	30	61
6	$PdBr_2$	DPEphos	DMSO	10	76[d–g]
7	$PdCl_2$	DPEphos	DMSO	10	62
8	PdI_2	DPEphos	DMSO	10	60
9	$Pd(OAc)_2$	DPEphos	DMSO	10	72
10	$Pd(acac)_2$	DPEphos	DMSO	10	40
11	$PdBr_2$	DPEphos	DMA	10	29
12	$PdBr_2$	DPEphos	mesitylene	10	22

[a]Reaction conditions: **1a** (1 equiv, 0.188 mmol), **2a** (2 equiv), [Pd] (5 mol %), ligand (20 mol %), and base (1 equiv) in solvent (2 mL) were heated in a sealed tube at the indicated temperature. [b]Yield of isolated **3a**. [c]10 mol % of DPEphos was used. [d]For control experiments, no conversion at all was observed in the absence of $PdBr_2$ or Ag_2CO_3. [e]Compound **3a** was formed in 60% yield when the reaction was carried out with $Pddba_2$ (5 mol %) instead of $PdBr_2$. [f]40% yield of **3a** was obtained when using only 5 mol % of $PdBr_2$ and 5 mol % of DPEPhos, and 66% yield of **3a** was obtained when using only 3 mol % of $PdBr_2$ and 20 mol % of DPEPhos. [g]Only 24% yield of **3a** was obtained when the reaction was carried out in a mixture of DMA:toluene (1.8 mL:0.2 mL) as the solvent.

yields regardless of the nature of the substituents on the aromatic ring of the quinolin-4-one 3-carboxylic acid or coumarin/quinolin-2-one moieties (compounds **3a–o**, Table 2). Under our optimal conditions, the reaction selectivity was investigated with coumarin and quinolin-2-one substrates containing two carbon–bromine bonds. The coupling proceeded at the more activated C-3 position and yielded the monocoupling products **3c**, **3h**, **3k**, and **3o** in good yields, without any trace of the side product arising from the coupling at 6-Br position. The selectivity of this procedure in the case of other heterocyclic substrates must be especially underlined, because the reaction with 3,5-dibromopyridinone gives only 3-quinoyl-5-bromopyridinone **3p** in a 63% yield. The presence of a carbon–halogen bond in **3c**, **3h**, **3k**, **3o**, and **3p** provided a handle for further structural diversifications using metal-catalyzed cross coupling reactions.

To further expand the scope of our methodology, we used this catalytic system in direct coupling of other heterocyclic carboxylic acids with various heterocyclic halides (Table 3). Overall, we were pleased with the generality of our protocol. The reactions proceeded in good yields with substituted naphthyridin-4-one, affording the corresponding 3-naphthyridin-4-one–coumarin biheterocycle **4a** with an acceptable 41% yield (Table 3). Remarkably, chrom-4-one 2-carboxylic acids and coumarin 3-carboxylic acids also undergo clean selective coupling with various halogenated heterocyclic compounds such as 3-bromoquinolin-2-ones, 3-bromocoumarins, and 3-iodoquinolinones as well as 3-bromopyridinones, providing the desired coupling products **4b–l** in yields ranging from 64% to 84%.

The proposed reaction mechanism is outlined in Scheme 2. The reaction starts with the extrusion of CO_2 from a silver carboxylate **A** which is generated from the carboxylic acid heterocycle and silver carbonate. The resulting intermediate **B** transfers its heterocycle group to a heterocyclepalladium(II) complex **C** generated by oxidative addition of a heterocycle bromide to a palladium catalyst, giving rise to a biheterocyclepalladium(II) species **D**. The catalytic cycle for the palladium is closed by reductive elimination of the bis-heterocycle, thus also regenerating the initial palladium(0) species.

3. CONCLUSION

In summary, we have reported a novel palladium-catalyzed direct decarboxylative coupling process to form a series of biheterocycle derivatives in good yields. This protocol exhibited broad substrate scope with respect to both the heterocyclic carboxylic acids and halide partners. It provides an attractive alternative to the existing methods for the synthesis of substituted biheterocycles of biological interests. We believe that this methodology should find broad applications in synthetic organic chemistry, as well as in the combinatorial and pharmaceutical sciences.

4. EXPERIMENTAL SECTION

General. All reactions were conducted under an argon atmosphere. Solvents: cyclohexane and ethyl acetate (EtOAc) for extraction and chromatography were technical grade. These compounds were all identified by the usual physical methods that are ^{1}H NMR, ^{13}C NMR (J-MOD), IR, and HR-MS (ESI or APCI). ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$. ^{1}H chemical shifts are reported in ppm from internal standard TMS or from residual chloroform (7.27 ppm). The following abbreviations are used: m (multiplet), s (singlet), bs (broad singlet), d (doublet), t (triplet), dd (doublet of doublet), td (triplet of doublet), q (quartet), qui (quintet), and sex (sextet). ^{13}C chemical shifts are reported in ppm from the central peak of deuteriochloroform (77.14). High-resolution mass spectra (HR-MS) were recorded on a MicroTOF spectrometer, using ESI or APCI with methanol as the carrier solvent. Nominal and exact m/z values are reported in Daltons. IR spectra were measured are reported in wave

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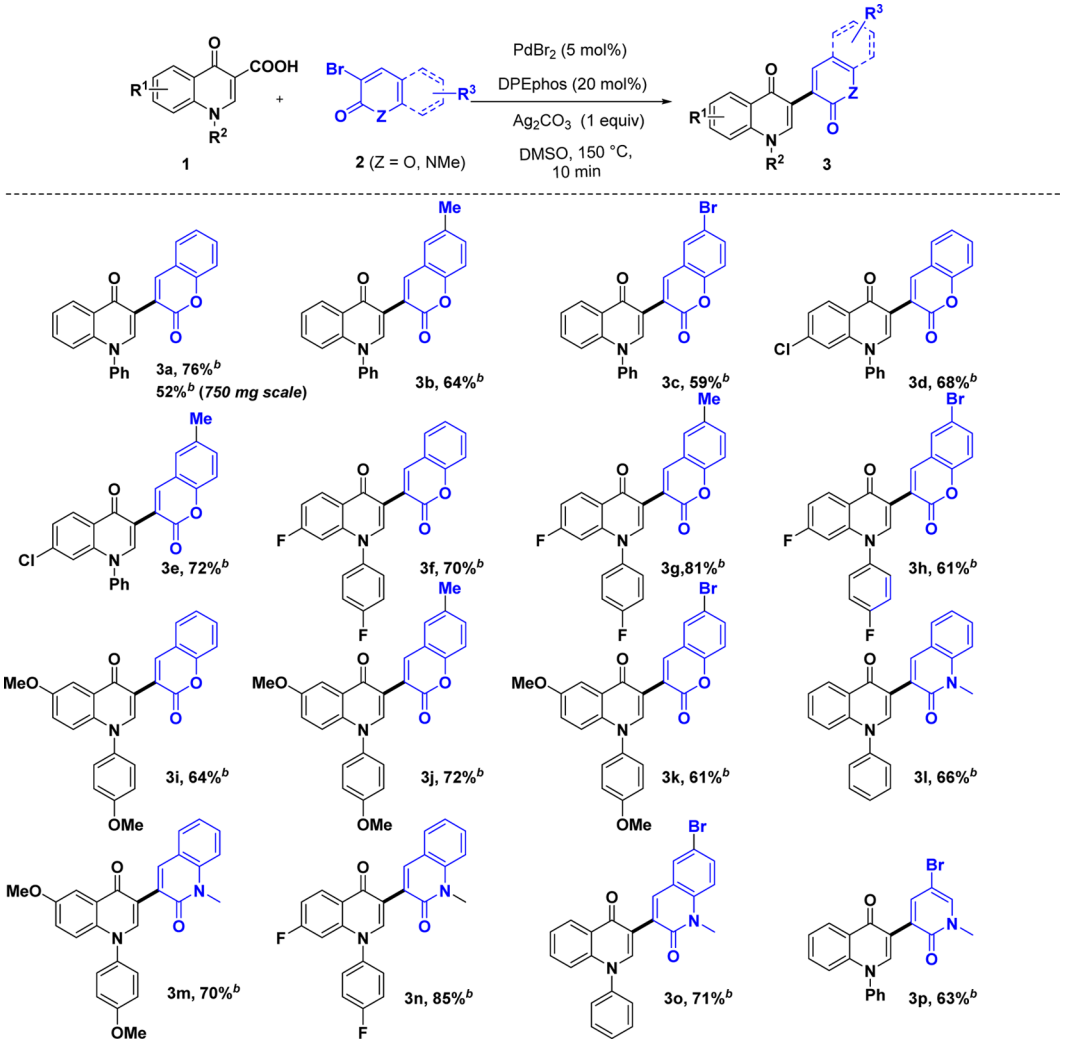
Table 2. Pd-Catalyzed Decarboxylative Coupling of Quinolinone 3-carboxylic Acids 1 with 3-Bromocoumarins and 3-Bromoquinolin-2(1*H*)-ones[a]



[a]To a solution of **1** (0.56 mmol) and **2** (2 equiv) in DMSO (2 mL) were added $PdBr_2$ (5.0 mol %), DPEphos (20 mol %), and Ag_2CO_3 (1 equiv). The reaction vessel was capped with a rubber septum, evacuated, and backfilled with argon. The reaction vessel was sealed, placed in the Emrys Optimizer, and exposed to microwave irradiation according to the following specifications: temperature: 150 °C; 10 min. [b]Yield of isolated products **3a–p**.

numbers (cm^{-1}). Analytical TLC was performed on precoated silica gel plates. Silica gel 60 (0.0150–0.040 mm) was used for flash chromatoghraphy. Carboxylic acids **1** are commercially available or prepared as reported in the literature.[11] 3-Bromocoumarins and 3-bromoquinolinones are prepared as reported in the literature.[12]

General Procedure for Decarboxylative Arylation of Quinolone-3-carboxylic Acid 1 and Related Heterocyclic Carboxylic Acid with Hetero Aryl Halides 2 under Microwave Irradiation. A flame-dried resealable 2–5 mL Pyrex reaction vessel was charged with the solid reactant(s): $PdBr_2$ (5.0 mol %), DPEphos (20 mol %), heterocyclic carboxylic acid (1 equiv), hetero aryl halide (2 equiv), and Ag_2CO_3 (1 equiv). The reaction vessel was capped with a rubber septum, evacuated, and backfilled with argon; this evacuation/backfill sequence was repeated one additional time. DMSO (2 mL) was added through the septum. The septum was replaced with a Teflon screwcap. The reaction vessel was sealed, placed in the Emrys Optimizer, and exposed to microwave irradiation according to the following specifications: temperature, 150 °C; 10 min; fixed hold time, on; high absorption, high; prestirring, 30 s. The resulting suspension was cooled to room temperature and filtered through a pad of Celite eluting with ethyl acetate, and the inorganic salts were removed. The crude reaction mixture was diluted with sat. aq NaCl solution (7.5 mL) and extracted with ethyl acetate (3 × 7.5 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated in vacuo. The organic layers were evaporated under reduced pressure, the resulting crude product was concentrated, and purification of the residue by silica gel column chromatography gave the desired product.

*3-(2-Oxo-2H-chromen-3-yl)-1-phenylquinolin-4(1H)-one (**3a**).*[8e] The reaction was carried out from 4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1a**[11c] and 3-bromocoumarin **2a**.[12a] Yield: 76% (155.4 mg, 0.56 mmol); white solid; mp: 249–251 °C; TLC: R_f 0.44 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 3064, 1717, 1619, 1609, 1585, 1548, 1477, 1451, 1373, 1344, 1321, 1279, 1255, 1195, 1160, 1122, 1099, 1028; ^1H NMR (300 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.77 (s, 1H), 8.58 (dd, J = 8.0, 1.3 Hz, 1H), 7.67–7.39 (m, 9H), 7.30 (dd, J = 10.7, 4.3 Hz, 2H), 7.07 (d, J = 8.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8 (C), 161.2 (C), 153.0 (C), 144.9 (CH), 142.3 (CH), 141.4 (C), 140.2 (C), 132.1 (CH), 131.1 (CH), 130.4 (2CH), 129.8 (CH), 128.4 (CH), 127.6 (2CH), 127.3 (CH), 126.7 (C), 124.6 (CH), 124.5 (CH), 120.0 (2C), 117.5 (CH), 116.2 (CH), 113.4 (C). HRMS (ESI): m/z calcd for $C_{24}H_{15}NO_3$ $(M + H)^+$ 366.1130, found: 366.1134.

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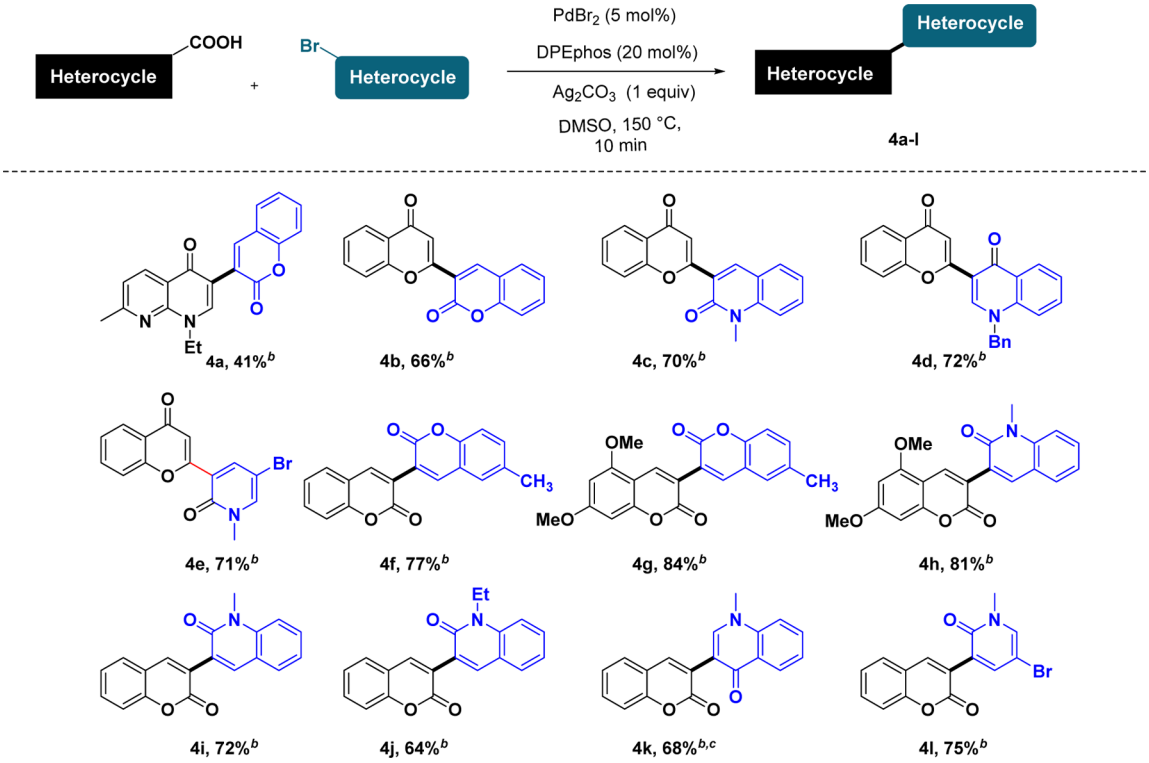
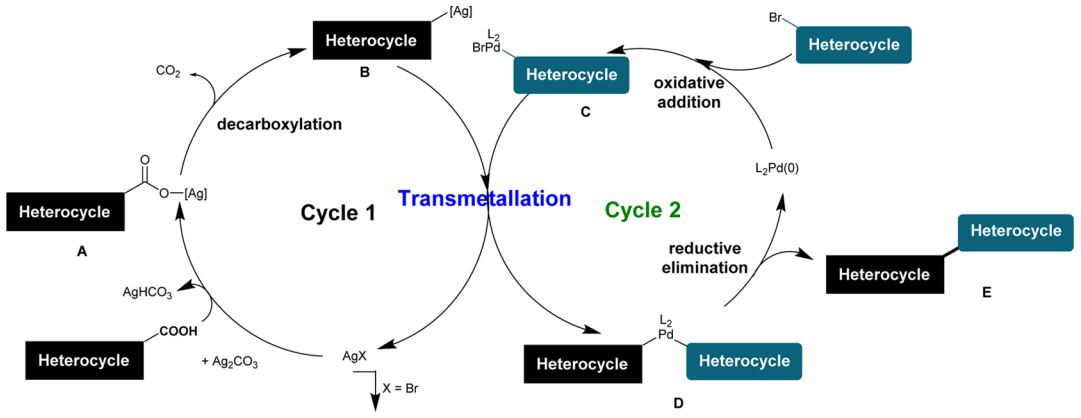
Table 3. Pd-Catalyzed Decarboxylative Coupling of Various Heterocyclic Carboxylic Acids with Substituted Heterocyclic Halides[a]



[a]To a solution of heterocycle carboxylic acid (0.56 mmol mmol) and heterocycle halide (2 equiv) in DMSO (2 mL) were added $PdBr_2$ (5.0 mol %), DPEphos (20 mol %), and Ag_2CO_3 (1 equiv). The reaction vessel was capped with a rubber septum, evacuated, and backfilled with argon. The reaction vessel was sealed, placed in the Emrys Optimizer, and exposed to microwave irradiation according to the following specifications: temperature: 150 °C; 10 min. [b]All yields given are of isolated products after column purification. [c]3-Iodoquinlone was used as the coupling partner.

Scheme 2. Proposed Mechanism for the Pd-Catalyzed Bis-heterocycle Synthesis



*3-(6-Methyl-2-oxo-2H-chromen-3-yl)-1-phenylquinolin-4(1H)-one (**3b**).* The reaction was carried out from 4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1a**[11c] and 3-bromo-6-methyl-2*H*-chromen-2-one **2b**.[12a] Yield: 64% (135.9 mg, 0.56 mmol); white solid; mp: 233−235 °C; TLC: R_f 0.37 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 1713, 1622, 1607, 1589, 1552, 1493, 1477, 1402, 1373, 1317, 1276, 1245, 1227, 1199, 1167, 1151, 1133, 1119, 1098, 1068, 1041, 1028, 1000; ^1H NMR (300 MHz, $CDCl_3$) δ ^1H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.79 (s, 1H), 8.61 (dd, J = 8.0, 1.3 Hz, 1H), 7.72−7.21 (m, 10H), 7.11 (d, J = 8.5 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8 (C), 161.3 (C), 151.1 (C), 144.8 (CH), 142.2 (CH), 141.3 (C), 140.1 (C), 134.0 (C), 132.1 (CH), 131.9 (CH), 130.3 (CH), 129.6 (CH), 128.1 (CH), 127.6 (2CH), 127.1 (CH), 126.6 (C), 124.4 (CH), 123.8 (CH), 119.8 (C), 119.7 (C), 117.4 (CH), 115.8 (CH), 113.4 (C), 20.9 (CH_3). HRMS (ESI): m/z calcd for $C_{25}H_{17}NO_3$ (M + H) $^+$ 380.1287, found: 380.1281.

*3-(6-Bromo-2-oxo-2H-chromen-3-yl)-1-phenylquinolin-4(1H)-one (**3c**).* The reaction was carried out from 4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1a**[11c] and 3,6-dibromo-2*H*-chromen-2-one **2c**.[12a] Yield: 59% (146.7 mg, 0.56 mmol); yellow solid; mp: 253−255 °C; TLC: R_f 0.45 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 3072, 1716, 1618, 1607, 1576, 1546, 1493, 1476, 1397, 1372, 1338, 1310, 1266, 1248, 1186, 1128, 1119, 1096, 1067, 1039, 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.76 (s, 1H), 8.56 (dd, J = 8.0, 1.5 Hz, 1H), 7.72 (d, J = 2.3 Hz, 1H), 7.67−7.37 (m, 8H), 7.20 (d, J = 8.8 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8 (C), 160.6 (C), 151.7 (C), 145.1 (CH), 141.3 (C), 140.5 (CH), 140.2 (C), 134.2 (CH), 133.7 (CH), 132.2 (CH), 130.5 (CH),

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130.5 (CH), 129.8 (CH), 127.6 (CH), 127.2 (CH), 126.7 (C), 124.7 (CH), 121.6 (C), 121.1 (2C), 117.9 (CH), 117.6 (CH), 117.1 (C), 112.9 (CH). HRMS (ESI): m/z calcd for $C_{24}H_{14}{}^{79}BrNO_3$ $(M + H)^+$ 444.0235, found: 444.0240. and m/z calcd for $C_{24}H_{14}{}^{81}BrNO_3$ $(M + H)^+$ 446.0055, found: 446.0052.

*7-Chloro-3-(2-oxo-2H-chromen-3-yl)-1-phenylquinolin-4(1H)-one (**3d**).* The reaction was carried out from 7-chloro-4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1b**[11d] and 3- bromocoumarin **2a**.[12a] Yield: 68% (135.9 mg, 0.50 mmol); white solid; mp: 253−255 °C; TLC: R_f 0.36 (*c*-hexane/EtOAc 30/70); IR (neat): ν (cm^{-1}) 3104, 2923, 2851, 1718, 1620, 1606, 1585, 1541, 1487, 1458, 1446, 1363, 1319, 1306, 1278, 1223, 1192, 1175, 1160, 1121, 1103, 1028, 1000; ^1H NMR (300 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.73 (s, 1H), 8.50 (d, J = 8.7 Hz, 1H), 7.70−7.56 (m, 4H), 7.49 (ddd, J = 7.5, 5.2, 1.5 Hz, 3H), 7.41−7.29 (m, 3H), 7.04 (d, J = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3 (C), 161.1 (C), 153.0 (C), 145.2 (CH), 142.5 (CH), 140.9 (C), 138.6 (C), 132.7 (C), 131.3 (CH), 130.7 (2CH), 130.1 (CH), 129.0 (CH), 128.5 (CH), 127.5 (2CH), 125.3 (CH), 125.0 (C), 124.6 (CH), 119.9 (C), 119.6 (C), 117.1 (CH), 116.3 (CH), 114.0 (C). HRMS (ESI): m/z calcd for $C_{24}H_{14}NO_3Cl$ $(M + H)^+$ 400.0740, found: 400.0738.

*7-Chloro-3-(6-methyl-2-oxo-2H-chromen-3-yl)-1-phenylquinolin-4(1H)-one (**3e**).* The reaction was carried out from 7-chloro-4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1b**[11d] and 3-bromo-6-methyl-2*H*-chromen-2-one **2b**.[12a] Yield: 72% (148.9 mg, 0.50 mmol); white solid; mp: 264−266 °C; TLC: R_f 0.32 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 3103, 3078, 2925, 1921, 1712, 1624, 1591, 1544, 1492, 1464, 1446, 1387, 1361, 1309, 1277, 1224, 1195, 1160, 1133, 1102, 1030, 1003; ^1H NMR (300 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.77 (s, 1H), 8.53 (d, J = 8.5 Hz, 1H), 7.77−7.15 (m, 10H), 7.08 (s, 1H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2 (C), 161.2 (C), 151.2 (C), 145.1 (CH), 142.4 (CH), 140.9 (C), 140.8 (C), 138.5 (C), 134.2 (C), 132.3 (CH), 130.6 (2CH), 130.0 (CH), 129.0 (CH), 128.2 (CH), 127.5 (2CH), 125.1 (CH), 125.0 (C), 119.6 (CH), 119.4 (C), 117.0 (C), 115.9 (CH), 114.1 (C), 20.9 (CH_3). HRMS (ESI): m/z calcd for $C_{25}H_{16}ClNO_3$ $(M + H)^+$ 414.0897, found: 414.0899.

*7-Fluoro-1-(4-fluorophenyl)-3-(2-oxo-2H-chromen-3-yl)quinolin-4(1H)-one (**3f**).* The reaction was carried out from 7-fluoro-1-(4-fluorophenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1c**[11a] and 3-bromocoumarin **2a**.[12a] Yield: 70% (137.6 mg, 0.49 mmol); white solid; mp: 249−251 °C; TLC: R_f 0.35 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 3065, 1688, 1615, 1558, 1506, 1485, 1374, 1339, 1323, 1280, 1246, 1218, 1199, 1160, 1147, 1121, 1094, 1018; ^1H NMR (300 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.70 (s, 1H), 8.14 (dd, J = 9.0, 2.9 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.51−7.41 (m, 3H), 7.35−7.17 (m, 5H), 7.00 (dd, J = 9.3, 4.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9 (C), 164.6 (C), 161.3 (C), 158.1 (C), 152.9 (C), 144.8 (CH), 142.4 (CH), 137.2 (C), 136.7 (C), 131.3 (CH), 129.6 (CH), 128.4 (CH), 128.1 (C), 128.0 (C), 124.6 (CH), 120.9 (CH), 120.6 (CH), 119.8 (C), 119.7 (CH), 119.6 (CH), 117.8 (CH), 116.2 (CH), 112.9 (C), 112.1 (CH). ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.75, −116.00. HRMS (ESI): m/z calcd for $C_{24}H_{13}NO_3F_2$ $(M + H)^+$ 402.0942, found: 402.0945.

*7-Fluoro-1-(4-fluorophenyl)-3-(6-methyl-2-oxo-2H-chromen-3-yl)quinolin-4(1H)-one (**3g**).* The reaction was carried out from 7-fluoro-1-(4-fluorophenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1c**[11a] and 3-bromo-6-methyl-2*H*-chromen-2-one **2b**.[12a] Yield: 81% (164.8 mg, 0.49 mmol); white solid; mp: 206−208 °C; TLC: R_f 0.43 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 3444, 3065, 2927, 2251, 1912, 1717, 1622, 1607, 1589, 1569, 1557, 1509, 1485, 1415, 1374, 1342, 1320, 1281, 1248, 1223, 1201, 1173, 1157, 1135, 1094, 1020; ^1H NMR (300 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.78 (d, J = 6.5 Hz, 1H), 8.22 (dd, J = 9.0, 3.0 Hz, 1H), 7.54 (ddd, J = 10.1, 5.1, 2.8 Hz, 2H), 7.44−7.18 (m, 6H), 7.08 (dd, J = 9.3, 4.3 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9 (C), 164.6 (C), 161.3 (C), 158.0 (C), 151.1 (C), 144.7 (CH), 142.5 (CH), 137.2 (C), 136.7 (C), 134.2 (C), 132.4 (CH), 129.6 (CH), 128.2 (C), 120.9 (CH), 120.6 (CH), 119.6 (C), 119.5 (CH), 119.4 (C), 117.7 CH), 117.4 (CH), 115.9 (CH), 113.0 (C), 112.1 (CH), 111.8 (CH), 20.9 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.82, −116.11. HRMS (ESI): m/z calcd for $C_{25}H_{15}NO_3F_2$ $(M + H)^+$ 416.1098, found: 416.1103; for $C_{25}H_{15}F_2NO_3$ $(M + Na)^+$ 438.0918, found: 438.0929.

*3-(6-Bromo-2-oxo-2H-chromen-3-yl)-7-fluoro-1-(4-fluorophenyl)-quinolin-4(1H)-one (**3h**).* The reaction was carried out from 7-fluoro-1-(4-fluorophenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1c**[11a] and 3,6-dibromo-2*H*-chromen-2-one **2c**.[12a] Yield: 61% (143.5 mg, 0.49 mmol); white solid; mp: 241−243 °C; TLC: R_f 0.48 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 2918, 2849, 2242,1715, 1612, 1581, 1553, 1505, 1485, 1405, 1373, 1342, 1314, 1221, 1197, 1152, 1129, 1089, 1066, 1015; ^1H NMR (300 MHz, $CDCl_3$) δ 8.95 (s, 1H), 8.74 (s, 1H), 8.19 (dd, J = 9.0, 2.9 Hz, 1H), 7.73 (d, J = 2.3 Hz, 1H), 7.58 (dd, J = 8.8, 2.3 Hz, 1H), 7.53−7.42 (m, 2H), 7.37−7.25 (m, 3H), 7.21 (d, J = 8.8 Hz, 1H), 7.03 (dd, J = 9.3, 4.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.9 (C), 164.7 (C), 161.4 (C), 160.5 (C), 158.2 (C), 151.7 (C), 145.0 (CH), 140.8 (CH), 137.1 (C), 136.7 (C), 134.0 (CH), 130.6 (CH), 129.6 (CH), 128.2 (C), 121.5 (C), 121.1 (CH), 120.8 (CH), 119.7 (CH), 118.0 (CH), 117.5 (C), 117.2 (CH), 112.5 (C), 112.2 (CH), 111.9 (CH). ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.59, −115.72. HRMS (ESI): m/z calcd for $C_{24}H_{12}NF_2O_3{}^{79}Br$ $(M + H)^+$ 480.0044, found: 480.0038 and $C_{24}H_{12}NF_2O_3{}^{81}Br$ $(M + H)^+$ 482.0013, found: 482.0017.

*6-Methoxy-1-(4-methoxyphenyl)-3-(2-oxo-2H-chromen-3-yl)-quinolin-4(1H)-one (**3i**).* The reaction was carried out from 6-methoxy-1-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1d**[11c] and 3-bromocoumarin **2a**.[12a] Yield: 64% (125.2 mg, 0.46 mmol); yellow solid; mp: 206−208 °C; TLC: R_f 0.60 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3079, 3007, 2988, 2954, 2910, 2832, 2062, 1702, 1612, 1579, 1554, 1511, 1488, 1436, 1382, 1353, 1322, 1303, 1282, 1265, 1234, 1217, 1197, 1184, 1168, 1157, 1120, 1093, 1037, 1019; ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.59 (s, 1H), 7.85 (d, J = 2.6 Hz, 1H), 7.57−7.12 (m, 6H), 7.08−6.86 (m,, 4H), 3.82 (d, J = 12.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2 (C), 161.3 (C), 160.3 (C), 156.9 (C), 153.0 (C), 144.3 (CH), 142.0 (CH), 135.2 (C), 134.2 (C), 131.0 (CH), 128.7 (2CH), 128.3 (CH), 127.9 (C), 124.5 (CH), 122.7 (CH), 120.3 (C), 120.1 (C), 119.4 (CH), 116.2 (CH), 115.4 (2CH), 112.3 (C), 106.0 (CH), 55.9 (CH_3), 55.84 (CH_3). HRMS (ESI): m/z calcd for $C_{26}H_{19}NO_5$ $(M + H)^+$ 426.1341, found: 426.1349.

*6-Methoxy-1-(4-methoxyphenyl)-3-(6-methyl-2-oxo-2H-chromen-3-yl)quinolin-4(1H)-one (**3j**).* The reaction was carried out from 6-methoxy-1-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1d**[11c] and 3-bromo-6-methyl-2*H*-chromen-2-one **2b**.[12a] Yield: 72% (145.5 mg, 0.46 mmol); white solid; mp: 230−232 °C; TLC: R_f 0.51 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3002, 2937, 2840, 2242, 1712, 1623, 1612, 1565, 1547, 1509, 1487, 1439, 1380, 1352, 1321, 1300, 1278, 1267, 1251, 1242, 1223, 1198, 1166, 1130, 1108, 1096, 1025; ^1H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.71 (s, 1H), 7.99 (d, J = 2.9 Hz, 1H), 7.53−6.99 (m, 9H), 3.96 (d, J = 13.4 Hz, 6H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2 (C), 161.5 (C), 160.2 (C), 156.8 (C), 151.1 (C), 144.6 (CH), 144.2 (CH), 142.1 (CH), 135.2 (C), 134.2 (C), 134.1 (C), 132.1 (CH), 128.7 (CH), 128.0 (CH), 127.8 (C), 122.7 (2CH), 120.2 (C), 119.8 (C), 119.3 (CH), 115.9 (CH), 115.3 (CH), 112.4 (C), 106.0 (CH), 55.9 (CH_3), 55.8 (CH_3), 20.9 (CH_3). HRMS (ESI): m/z calcd for $C_{27}H_{21}NO_5$ $(M + H)^+$ 440.1487, found: 440.1490.

*3-(6-Bromo-2-oxo-2H-chromen-3-yl)-6-methoxy-1-(4-methoxyphenyl)quinolin-4(1H)-one (**3k**).* The reaction was carried out from 6-methoxy-1-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1d**[11c] and 3,6-dibromo-2*H*-chromen-2-one **2c**.[12a] Yield: 61% (141.5 mg, 0.46 mmol); yellow solid; mp: 255−257 °C; TLC: R_f 0.81 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 2998, 2837, 1716, 1628, 1610, 1601, 1582, 1552, 1510, 1487, 1452, 1437, 1407, 1374, 1348, 1320, 1301, 1268, 1249, 1210, 1194, 1163, 1137, 1096, 1067, 1036, 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.60 (d, J = 1.3 Hz, 1H), 7.84 (s, 1H), 7.60 (s, 1H), 7.46 (d, J = 8.7 Hz, 1H), 7.39−6.82 (m, 7H), 3.83 (dd, J = 12.3, 1.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0 (C), 160.5 (C), 160.2 (C), 156.9 (C), 151.6 (C), 144.3 (2CH), 140.2 (CH), 135.0 (C), 134.0 (C), 133.5 (CH), 130.3 (CH), 128.54 (CH), 127.7 (C), 122.7 (2CH), 121.6 (C), 121.4 (C), 119.3 (CH), 117.7 (CH), 116.9 (C), 115.2

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(CH), 111.7 (C), 105.9 (CH), 55.8 (CH_3), 55.7 (CH_3). HRMS (ESI): m/z calcd for $C_{26}H_{18}NO_5{}^{79}Br$ $(M + H)^+$ 504.0447, found: 504.0446 and m/z calcd for $C_{26}H_{18}NO_5{}^{81}Br$ $(M + H)^+$ 506.0426, found: 506.0432.

1-Methyl-1′-phenyl-[3,3′-biquinoline]-2,4′(1H,1′H)-dione (**3l**). The reaction was carried out from 4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1a**[11c] and 3-bromo-1-methylquinolin-2(1*H*)-one **2d**.[12b] Yield: 66% (139.8 mg, 0.56 mmol); white solid; mp: 218−220 °C; TLC: R_f 0.26 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 2923, 1621, 1583, 1548, 1493, 1476, 1452, 1401, 1372, 1333,1318, 1292, 1236, 1198, 1165, 1104, 1062; ^1H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, J = 8.8 Hz, 2H), 8.58 (dt, J = 12.3, 6.1 Hz, 1H), 7.68 (dd, J = 7.8, 1.3 Hz, 1H), 7.64−7.46 (m, 7H), 7.38 (ddd, J = 15.6, 11.3, 4.8 Hz, 2H), 7.23 (dd, J = 10.9, 3.7 Hz, 1H), 7.06 (d, J = 8.0 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0 (C), 161.9 (C), 144.9 (CH), 141.6 (C), 140.3 (C), 139.3 (CH), 139.1 (C), 131.7 (CH), 130.3 (2CH), 130.2 (CH), 129.5 (CH), 129.4 (CH), 127.7 (2CH), 127.3 (CH), 126.9 (C), 124.1 (CH), 123.9 (C), 122.3 (CH), 121.0 (C), 117.4 (CH), 115.2 (C), 113.9 (CH), 30.2 (CH_3). HRMS (ESI): m/z calcd for $C_{25}H_{18}N_2O_2$ $(M + H)^+$ 379.1447, found: 379.1450.

6′-Methoxy-1′-(4-methoxyphenyl)-1-methyl-[3,3′-biquinoline]-2,4′(1H,1′H)-dione (**3m**). The reaction was carried out from 6-methoxy-1-(4-methoxyphenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1d**[11c] and 3-bromo-1-methylquinolin-2(1*H*)-one **2d**.[12b] Yield: 70% (141.1 mg, 0.46 mmol); white solid; mp: 231−233 °C; TLC: R_f 0.18 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3117, 3079, 3010, 2934, 2837, 1630, 1612, 1584, 1547, 1512, 1490, 1458, 1435, 1414, 1374, 1350, 1328, 1292, 1267, 1252, 1232, 1212, 1187, 1163, 1099, 1060, 1022^1H NMR (300 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.75 (s, 1H), 8.01 (d, J = 2.9 Hz, 1H), 7.66 (t, J = 12.7 Hz, 1H), 7.62−7.50 (m, 1H), 7.40 (dt, J = 13.9, 5.9 Hz, 3H), 7.27 (dd, J = 13.5, 5.9 Hz, 1H), 7.21−6.98 (m, 4H), 3.96 (s, 3H), 3.91 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.3 (C), 161.9 (C), 160.1 (C), 156.5 (C), 144.4 (CH), 139.1 (CH), 139.0 (C), 135.3 (C), 134.4 (C), 130.0 (CH), 129.2 (CH), 128.7 (2CH), 127.9 (C), 124.2 (C), 122.3 (CH), 122.2 (CH), 121.0 (C), 119.2 (CH), 115.2 (2CH), 114.1 (C), 113.8 (CH), 106.0 (CH), 55.8 (CH_3), 55.7 (CH_3), 30.1 (CH_3). HRMS (ESI): m/z calcd for $C_{27}H_{22}N_2O_4$ $(M + H)^+$ 439.1658, found: 439.1663

7′-Fluoro-1′-(4-fluorophenyl)-1-methyl-[3,3′-biquinoline]-2,4′(1H,1′H)-dione (**3n**). The reaction was carried out from 7-fluoro-1-(4-fluorophenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylic acid **1c**[11a] and 3-bromo-1-methylquinolin-2(1*H*)-one **2d**.[12b] Yield: 85% (172.5 mg, 0.49 mmol); white solid; mp: 251−253 °C; TLC: R_f 0.44 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3035, 2919, 2851, 1638, 1615, 1588, 1561, 1503, 1484, 1461, 1417, 1393, 1372, 1354, 1334, 1317, 1296, 1259, 1243, 1215, 1202, 1163,1101, 1039, 1015; ^1H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, J = 2.3 Hz, 2H), 8.16 (dd, J = 9.1, 3.0 Hz, 1H), 7.64 (dd, J = 7.8, 1.1 Hz, 1H), 7.56−7.41 (m, 3H), 7.37−7.15 (m, 5H), 6.98 (dd, J = 9.3, 4.3 Hz, 1H), 3.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1 (C), 164.5 (C), 161.8 (C), 161.1 (C), 157.9 (C), 144.9 (CH), 139.4 (CH), 139.1 (C), 136.9 (C), 130.3 (CH), 129.7 (CH), 129.4 (CH), 128.2 (C), 123.4 (C), 122.4 (CH), 120.9 (C), 120.6 (CH), 119.5 (CH), 117.6 (CH), 117.3 (CH), 114.7 (C), 113.9 (CH), 112.1 (CH), 111.8 (CH), 30.1 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.25, −116.73. HRMS (ESI): m/z calcd for $C_{25}H_{16}N_2F_2O_2$ $(M + H)^+$ 415.1258, found: 415.1254.

6-Bromo-1-methyl-1′-phenyl-[3,3′-biquinoline]-2,4′(1H,1′H)-dione (**3o**). The reaction was carried out from 4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1a**[11c] and 3,6-dibromo-1-methylquinolin-2(1*H*)-one **2e**.[12c] Yield: 71% (150.4 mg, 0.56 mmol); white solid; mp: 289−291 °C; TLC: R_f 0.37 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3076, 1621, 1587, 1575, 1547, 1492, 1475, 1449, 1412, 1395, 1368, 1337, 1313, 1290, 1265, 1251, 1236, 1220, 1199, 1161, 1122, 1104, 1084, 1072, 1038, 1023, 1002; ^1H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.70 (s, 1H), 8.56 (dd, J = 8.0, 1.5 Hz, 1H), 7.77 (d, J = 2.2 Hz, 1H), 7.64−7.44 (m, 7H), 7.43−7.32 (m, 1H), 7.19 (d, J = 9.0 Hz, 1H), 7.05 (d, J = 8.4 Hz, 1H), 3.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8 (C), 161.5 (C), 145.0 (CH), 141.5 (C), 140.2 (C), 137.9 (C), 137.7 (CH), 132.7 (CH), 131.8 (CH), 131.2 (CH), 130.3 (2CH), 129.5 (CH), 127.6 (2CH), 127.3 (CH), 126.8 (C), 125.1 (C), 124.2 (CH), 122.5 (C), 117.4 (CH), 115.5 (CH), 115.0 (C), 114.7 (C), 30.3 (CH_3). HRMS (ESI): m/z calcd for $C_{25}H_{17}N_2O_2{}^{79}Br$ $(M + H)^+$ 457.0552, found: 457.0559 and m/z calcd for $C_{25}H_{17}N_2O_2{}^{81}Br$ $(M + H)^+$ 459.0531, found: 459.0552.

3-(5-Bromo-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-1-phenylquinolin-4(1H)-one (**3p**). The reaction was carried out from 4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid **1a**[11c] and 3,5-dibromo-1-methylpyridin-2(1*H*)-one **2f**.[12d] Yield: 63% (143.6 mg, 0.56 mmol); yellow solid; mp: 273−275 °C; TLC: R_f 0.26 (*c*-hexane/EtOAc 20/80); IR (neat): ν (cm^{-1}) 3057, 1775, 1636, 1619, 1603, 1586, 1570, 1548, 1533, 1493, 1478, 1448, 1422, 1404, 1367, 1348, 1317, 1304, 1247, 1207, 1155, 1120, 1089, 1073, 1038, 1001; ^1H NMR (300 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.66 (d, J = 2.7 Hz, 1H), 8.53 (dd, J = 8.0, 1.5 Hz, 1H), 7.62−7.32 (m, 8H), 7.03 (d, J = 8.5 Hz, 1H), 3.54 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7 (C), 160.7 (C), 144.8 (CH), 142.2 (CH), 141.5 (C), 140.2 (C), 136.0 (CH), 131.7 (CH), 130.3 (2CH), 129.5 (CH), 127.6 (2CH), 127.2 (CH), 126.8 (C), 124.7 (C), 124.2 (CH), 117.4 (CH), 113.9 (C), 98.7 (CH), 38.5 (CH_3). HRMS (ESI): m/z calcd for $C_{21}H_{15}{}^{79}BrN_2O_2$ $(M + H)^+$ 407.0395, found: 407.0400 and m/z calcd for $C_{21}H_{15}{}^{81}BrN_2O_2$ $(M + H)^+$ 409.0375, found: 409.0385.

1-Ethyl-7-methyl-3-(2-oxo-2H-chromen-3-yl)-1,8-naphthyridin-4(1H)-one (**4a**). The reaction was carried out from 1-ethyl-7-methyl-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxylic acid (commercially available) and 3-bromocoumarin **2a**.[12a] Yield: 41% (87.2 mg, 0.64 mmol); white solid; mp: 220−222 °C; TLC: R_f 0.515 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3086, 2965, 2919, 2849, 1714, 1619, 1604, 1573, 1540, 1498, 1485, 1444, 1375, 1347, 1316, 1263, 1234, 1184, 1151, 1136, 1118, 1098, 1052, 1021; ^1H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 8.88 (s, 1H), 8.67 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.51 (t, J = 7.7 Hz, 1H), 7.32 (dd, J = 18.3, 7.9 Hz, 3H), 4.55 (q, J = 7.1 Hz, 2H), 2.69 (s, 3H), 1.51 (d, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2 (C), 173.4 (C), 162.5 (C), 161.3 (C), 152.9 (C), 148.0 (C), 144.6 (C), 141.9 (CH), 136.6 (CH), 136.0 (CH), 131.1 (CH), 128.4 (CH), 124.5 (CH), 120.5 (C), 120.0 (CH), 116.2 (CH), 114.1 (C), 46.4 (CH_2), 30.4 (CH_3), 15.4 (CH_3). HRMS (ESI): m/z calcd for $C_{20}H_{16}N_2O_3$ $(M + H)^+$ 333.1239, found: 333.1233.

2′H,4H-[2,3′-Bichromene]-2′,4-dione(**4b**). The reaction was carried out from 4-oxo-4*H*-chromene-2-carboxylic acid (commercially available) and 3-bromocoumarin **2a**.[12a] Yield: 66% (149.4 mg, 0.78 mmol); white solid; mp: 243−245 °C; TLC: R_f 0.14 (*c*-hexane/EtOAc70/30); IR (neat): ν (cm^{-1}); 3064, 1722, 1701, 1633, 1608, 1563, 1488, 1465, 1450, 1397, 1349, 1330, 1280, 1244, 1208, 1187, 1163, 1136, 1120, 1092, 1026: ^1H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J = 7.0 Hz, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.75−7.54 (m, 5H), 7.47−7.29 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.5 (C), 156.6 (C), 156.2 (C), 154.1 (C), 143.8 (CH), 142.8 (CH), 134.1 (CH), 134.0 (CH), 129.4 (CH), 126.0 (CH), 125.4 (CH), 125.2 (CH), 124.0 (2C), 118.4 (C), 117.8 (CH), 116.8 (CH), 112.9 (CH). HRMS (ESI): m/z calcd for $C_{18}H_{10}O_4$ $(M + H)^+$ 291.0657, found: 291.0666.

1-Methyl-3-(4-oxo-4H-chromen-2-yl)quinolin-2(1H)-one (**4c**). The reaction was carried out from 4-oxo-4*H*-chromene-2-carboxylic acid (commercially available) and 3-bromo-1-methylquinolin-2(1*H*)-one **2d**.[12b] Yield: 70% (165.4 mg, 0.78 mmol); yellow solid; mp: 249−251 °C; TLC: R_f 0.35 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}): 1651, 1632, 1612, 1597, 1586, 1566, 1497, 1473, 1454, 1415, 1392, 1351, 1328, 1305, 1233, 1198, 1167, 1126, 1104, 1056, 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.20 (dt, J = 10.3, 5.2 Hz, 1H), 7.88 (s, 1H), 7.78−7.64 (m, 3H), 7.56 (dd, J = 8.4, 0.7 Hz, 1H), 7.43−7.28 (m, 3H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.9 (C), 159.3 (C), 158.3 (C), 156.3 (C), 140.5 (C), 139.2 (CH), 133.7 (CH), 132.8 (CH), 130.5 (CH), 125.9 (CH), 125.0 (CH), 124.1 (C), 122.8 (C), 122.2 (CH), 119.4 (C), 117.93(CH), 114.4 (CH), 112.9 (CH), 30.1 (CH_3). HRMS (ESI): m/z calcd for $C_{19}H_{13}NO_3$ $(M + H)^+$ 304.0974, found: 304.0981.

1-Benzyl-3-(4-oxo-4H-chromen-2-yl)quinolin-4(1H)-one (**4d**). The reaction was carried out from 4-oxo-4*H*-chromene-2-carboxylic acid (commercially available) and 1-benzyl-3-bromoquinolin-4(1*H*)-one **2g**.[12c] Yield: 72% (212.9 mg, 0.78 mmol); white solid; mp: 273−

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275 °C; TLC: R_f 0.16 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 2917, 2849, 2360, 1637, 1605, 1583, 1562, 1546, 1486, 1451, 1429, 1408, 1351, 1320, 1265, 1227, 1187, 1129, 1060, 1024; ^1H NMR (300 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.65−8.51 (m, 2H), 8.08 (s, 1H), 7.71−7.47 (m, 2H), 7.46−7.18 (m, 9H), 5.51 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.6 (C), 159.7 (C), 158.6 (C), 155.8 (C), 145.9 (CH), 143.9 (CH), 139.5 (C), 138.8 (C), 135.6 (C), 134.3 (C), 133.3 (CH), 129.6 (CH), 129.2 (CH), 128.8 (CH), 128.2 (CH), 127.9 (CH), 127.4 (CH), 126.4 (CH), 125.9 (CH), 125.2 (CH), 124.8 (CH), 117.5 (CH), 111.6 (C), 110.6 (CH), 57.7 (CH_2). HRMS (ESI): *m*/*z* calcd for $C_{25}H_{17}NO_3$ (M + H)$^+$ 380.1287, found: 380.1291.

5-Bromo-1-methyl-3-(4-oxo-4H-chromen-2-yl)pyridin-2(1H)-one ***(4e)***. The reaction was carried out from 4-oxo-4*H*-chromene-2-carboxylic acid (commercially available) and 3,5-dibromo-1-methylpyridin-2(1*H*)-one **2f**.[12d] Yield: 71% (183.9 mg, 0.78 mmol); yellow solid; mp: 212−214 °C; TLC: R_f 0.32 (*c*-hexane/EtOAc 30/70); IR (neat): ν (cm^{-1}) 3056, 2918, 1656, 1630, 1596, 1580, 1564, 1533, 1527, 1470, 1433, 1416, 1394, 1377, 1352, 1301, 1278, 1234, 1205, 1157, 1127, 1068; ^1H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 2.8 Hz, 1H), 8.21 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.92 (s, 1H), 7.67 (dt, *J* = 4.8, 1.7 Hz, 2H), 7.57−7.48 (m, 1H), 7.44−7.34 (m, 1H), 3.65 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.8 (C), 158.4 (C), 157.0 (C), 141.8 (C), 140.7 (CH), 133.9 (CH), 125.9 (CH), 125.2 (CH), 124.1 (C), 122.1 (C), 119.1 (C), 117.8 (CH), 112.4 (CH), 97.1 (CH), 38.8 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{15}H_{10}{}^{79}BrNO_3$ (M + H)$^+$ 331.9922, found: 331.9929 and *m*/*z* calcd for $C_{15}H_{10}{}^{81}BrNO_3$ (M + H)$^+$ 333.9902, found: 333.9909.

6-Methyl-2H,2′H-[3,3′-bichromene]-2,2′-dione ***(4f)***. The reaction was carried out from 2-oxo-2*H*-chromene-3-carboxylic acid (commercially available) and 3-bromo-6-methyl-2*H*-chromen-2-one **2b**.[12a] Yield: 77% (182.7 mg, 0.78 mmol); white solid; mp: 244−246 °C; TLC: R_f 0.40 (*c*-hexane/EtOAc70/30); IR (neat): ν (cm^{-1}) 2957, 2923, 2853, 1729, 1690, 1622, 1605, 1567, 1491, 1458, 1363, 1346, 1307, 1277, 1249, 1221, 1172, 1157, 1125, 1080; ^1H NMR (300 MHz, $CDCl_3$) δ 8.55 (d, *J* = 15.8 Hz, 2H), 7.57 (dd, *J* = 13.9, 7.2 Hz, 2H), 7.45−7.18 (m, 5H), 2.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.41 (C), 160.2 (C), 153.4 (C), 151.6 (C), 143.8 (CH), 143.7 (CH), 134.5 (C), 133.5 (CH), 133.5 (CH), 132.4 (CH), 128.9 (CH), 124.8 (CH), 120.3 (C), 120.0 (C), 119.2 (C), 118.9 (C), 116.5 (CH), 116.2 (CH), 20.9 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{19}H_{12}O_4$ (M + H)$^+$ 305.0814, found: 305.0819.

5,7-Dimethoxy-6′-methyl-2H,2′H-[3,3′-bichromene]-2,2′-dione ***(4g)***. The reaction was carried out from 5,7-dimethoxy-2-oxo-2*H*-chromene-3-carboxylic acid **1e**[11b] and 3-bromo-6-methyl-2*H*-chromen-2-one **2b**.[12a] Yield: 84% (180.5 mg, 0.59 mmol); white solid; mp: 229−231 °C; TLC: R_f 0.62 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 2956, 2923, 2853, 1728, 1714, 1632, 1619, 1605, 1581, 1566, 1494, 1471, 1417, 1365, 1341, 1306, 1294, 1257, 1207, 1155, 1114, 1081, 1044, 1000; ^1H NMR (300 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.41 (s, 1H), 7.40−7.30 (m, 2H), 7.30−7.20 (m, 1H), 6.44 (d, *J* = 2.1 Hz, 1H), 6.30 (d, *J* = 2.2 Hz, 1H), 3.89 (dd, *J* = 10.3, 2.4 Hz, 6H), 2.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.3 (C), 160.6 (C), 160.4 (C), 157.6 (C), 156.1 (C), 151.3 (C), 142.5 (CH), 139.1 (CH), 134.2 (C), 132.8 (CH), 128.2 (CH), 120.9 (C), 119.0 (C), 116.0 (CH), 114.8 (C), 104.4 (C), 95.0 (CH), 92.3 (CH), 56.0 (CH_3), 55.8 (CH_3), 20.7 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{21}H_{16}O_6$ (M + H)$^+$ 365.1025, found: 365.1033.

3-(5,7-Dimethoxy-2-oxo-2H-chromen-3-yl)-1-methylquinolin-2(1H)-one ***(4h)***. The reaction was carried out from 5,7-dimethoxy-2-oxo-2*H*-chromene-3-carboxylic acid **1e**[11b] and 3-bromo-1-methylquinolin-2(1*H*)-one **2d**.[12b] Yield: 81% (173.6 mg, 0.59 mmol); yellow solid; mp: 251−253 °C; TLC: R_f 0.45 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 1721, 1648, 1610, 1593, 1564, 1495, 1469, 1452, 1424, 1371, 1345, 1306, 1286, 1254, 1237, 1227, 1199, 1155, 1140, 1116, 1085, 1044, 1025; ^1H NMR (300 MHz, $CDCl_3$) δ 8.64 (d, *J* = 7.1 Hz, 1H), 8.25 (s, 1H), 7.68−7.47 (m, 2H), 7.32 (t, *J* = 12.4 Hz, 1H), 7.23 (dd, *J* = 11.8, 4.5 Hz, 1H), 6.43 (d, *J* = 2.1 Hz, 1H), 6.28 (d, *J* = 2.2 Hz, 1H), 3.87 (d, *J* = 7.8 Hz, 6H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9 (C), 161.1 (C), 161.0 (C), 157.5 (C), 156.3 (C), 139.5 (C), 139.1 (CH), 138.7 (CH), 130.8 (CH), 129.4 (CH), 125.5 (C), 122.3 (CH), 120.3 (C), 117.2 (C), 114.0 (CH), 104.6 (C), 94.9 (CH), 92.4 (CH), 56.0 (CH_3), 55.9 (CH_3), 30.1 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{21}H_{17}NO_5$ (M + H)$^+$ 364.1185, found: 364.1191.

1-Methyl-3-(2-oxo-2H-chromen-3-yl)quinolin-2(1H)-one ***(4i)***. The reaction was carried out from 2-oxo-2*H*-chromene-3-carboxylic acid (commercially available) and 3-bromo-1-methylquinolin-2(1*H*)-one **2d**.[12b] Yield: 72% (170.3 mg, 0.78 mmol); white solid; mp: 210−213 °C; TLC: R_f 0.22 (*c*-hexane/EtOAc70/30); IR (neat): ν (cm^{-1}): 1719, 1641, 1619, 1592, 1564, 1487, 1446, 1416, 1352, 1294, 1271, 1237, 1222, 1205, 1155,1 139, 1121, 1088, 1031, 1022; ^1H NMR (300 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.32 (s, 1H), 7.69−7.47 (m, 4H), 7.43−7.21 (m, 4H), 3.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0 (C), 160.5 (C), 153.5 (C), 143.2 (CH), 139.9 (C), 139.7 (CH), 131.8 (CH), 131.3 (CH), 129.7 (CH), 128.5 (CH), 124.7 (C), 124.5 (CH), 122.5 (CH), 120.1 (2C), 119.4 (C), 116.4 (CH), 114.1 (CH), 30.2 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{19}H_{13}NO_3$ (M + H)$^+$ 304.0974, found: 304.0986

1-Ethyl-3-(2-oxo-2H-chromen-3-yl)quinolin-2(1H)-one ***(4j)***. The reaction was carried out from 2-oxo-2*H*-chromene-3-carboxylic acid (commercially available) and 3-bromo-1-ethylquinolin-2(1*H*)-one **2h**.[12d] Yield: 64% (158.4 mg, 0.78 mmol); yellow solid; mp: 217−219 °C; TLC: R_f 0.28 (*c*-hexane/EtOAc 70/30); IR (neat): ν (cm^{-1}) 2961, 2925, 2853, 1720, 1641, 1619, 1591, 1562, 1486, 1462, 1443, 1371, 1349, 1293, 1276, 1241, 1221, 1198, 1156, 1138, 1123, 1084, 1038; ^1H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.35 (s, 1H), 7.72−7.46 (m, 4H), 7.43−7.20 (m, 4H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5 (C), 153.5 (C), 143.3 (CH), 140.0 (CH), 138.7(C), 131.7 (CH), 131.2 (CH), 130.0 (CH), 128.5 (CH), 124.5 (CH), 124.3 (C), 122.3 (CH), 120.4 (2C), 119.4 (2C), 116.4 (CH), 113.9 (CH), 38.2 (CH_2), 12.7 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{20}H_{15}NO_3$ (M + H)$^+$ 318.1130, found: 318.1137.

1-Methyl-3-(2-oxo-2H-chromen-3-yl)quinolin-4(1H)-one ***(4k)***. The reaction was carried out from 2-oxo-2*H*-chromene-3-carboxylic acid (commercially available) and 3-iodo-1-methylquinolin-4(1*H*)-one **2i**.[12b] Yield: 68% (160.8 mg, 0.78 mmol); white solid; mp: 214−216 °C; TLC: R_f 0.42 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 3062, 2360, 1714, 1 628, 1612, 1583, 1552, 1501, 1476, 1455, 1411, 1379, 1342, 1327, 1277, 1253, 1242, 1200, 1157, 1141, 1121, 1101, 1039; ^1H NMR (300 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.73 (s, 1H), 8.55 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.71 (ddd, *J* = 8.7, 7.1, 1.6 Hz, 1H), 7.58 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.53−7.40 (m, 3H), 7.28 (ddd, *J* = 7.5, 5.8, 4.8 Hz, 2H), 3.91 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8 (C), 161.5 (C), 152.9 (C), 145.9 (CH), 142.0 (CH), 139.4 (C), 132.4 (CH), 131.0 (CH), 128.4 (CH), 127.6 (CH), 127.2 (C), 124.5 (CH), 124.5 (CH), 120.1 (C), 120.0 (C), 116.2 (CH), 115.5 (CH), 113.0 (C), 41.5 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{19}H_{13}NO_3$ (M + H)$^+$ 304.0974, found: 304.0976.

5-Bromo-1-methyl-3-(2-oxo-2H-chromen-3-yl)pyridin-2(1H)-one ***(4l)***. The reaction was carried out from 2-oxo-2*H*-chromene-3-carboxylic acid (commercially available) and 3,5-dibromo-1-methylpyridin-2(1*H*)-one **2f**.[12d] Yield: 75% (194.3 mg, 0.78 mmol); white solid; mp: 223−225 °C; TLC: R_f 0.45 (*c*-hexane/EtOAc 50/50); IR (neat): ν (cm^{-1}) 1718, 1649, 1609, 1587, 1536, 1456, 1419, 1347, 1301, 1232, 1210, 1163, 1127, 1042, 1016; ^1H NMR (300 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.17 (d, *J* = 2.7 Hz, 1H), 7.52 (dd, *J* = 14.2, 5.1 Hz, 3H), 7.41−7.19 (m, 2H), 3.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.2 (C), 153.5 (C), 143.3 (CH), 143.1 (CH), 138.1 (CH), 132.0 (CH), 128.7 (CH), 124.9 (C), 124.6 (CH), 121.1 (C), 119.3 (C), 116.4 (CH), 97.8 (C), 38.7 (CH_3). HRMS (ESI): *m*/*z* calcd for $C_{15}H_{10}{}^{79}BrNO_3$ (M + H)$^+$ 331.9922, found: 331.9922 and *m*/*z* calcd for $C_{15}H_{10}{}^{81}BrNO_3$ (M + H)$^+$ 333.9902, found: 333.9901.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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^{1}H and ^{13}C NMR spectra of new compounds **3a−p** and **4a−l** (PDF)

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Notes

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