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Amination

Regioselective Synthesis of Quinazolinone-/Phenanthridine-Fused Heteropolycycles by Pd-Catalyzed Direct Intramolecular Aerobic Oxidative C–H Amination from Aromatic Strained Amides

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Abstract: A new route for the expedient synthesis of specific regioisomer of quinazolinone- and phenanthridine-fused heterocycles through a palladium-catalyzed regioselective intramolecular oxidative C–H amination from cyclic strained amides of aromatic amido–amidine systems (quinazolinones) has been developed. The amine functionalization of an aromatic C–H bond from a strained amide nitrogen involved in aromaticity has been a challenging work so far. The fusion of two heterocyclic cores, quinazolinone and phenanthridine, can occur in two different ways (linear and angular), but under the conditions reported here, only linear type isomer is exclusively produced. This approach provides a variety of substituted quinazolinone- and phenanthridine-fused derivatives in moderate to excellent yields. Moreover, such fused molecules show excellent fluorescent properties and have great potential to be a new type of fluorophores for the use in medicinal and material science.

Introduction

Transition-metal-catalyzed C–H bond functionalization is a useful tool to construct new heterocycles. Recent studies reveal different types of transformations for the conversion of C–H bond to C–C, C–N, C–O functionalities.[1] Thus, the development of transition-metal-catalyzed new oxidation systems for the C–H functionalization represents a central challenge to construct various types of N-heterocycles, including the fused motifs. Recently, N-fused heterocycles have drawn substantial attention due to their existence as utmost important structural motifs in several natural products, electroluminescent materials, and bioactive molecules.[2] Therefore, a synthesis of new N-fused scaffolds by a short synthetic route is in high demand for various kinds of interests, especially for the therapeutic targets in the pharmaceutical sectors worldwide. In an effort to synthesize N-fused heterocycles by a transition-metal-catalyzed C–H functionalization, our interest was to make annulated quinazolinone- and phenanthridine-fused heterocycles amenable by a short and efficient synthetic methodology. Among the nitrogen-containing heterocycles, quinazolinones belong to a privileged class due to their wide range of biological and pharmacological activities, such as diuretic,[3] anti-inflammatory,[4] antidiabetic,[5] anti-hepatitis C,[6] anticonvulsant,[7] antileshmanial,[8] anticancer[9] and so forth. This motif is also very much abundant in various types of natural products, like Luotonin A,[10] Isaindigotone,[11] Tryptanthrin,[12] and Circumdatin H[13] (Figure 1).

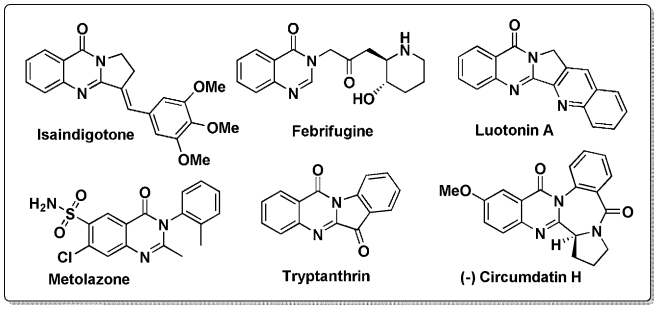

Figure 1. Structures of some bioactive molecules containing fused quinazolinone.

On the other hand, Phenanthridine is considered as another significant N-heterocyclic scaffold due to its biological activity and existence in several natural products.[14] This heterocycle is a basic functional moiety for DNA binding fluorescent probes (Figure 2), due to its intercalating property.[15] A recent report has revealed that phenanthridine derivatives may be used as radiotracers for imaging of brain 5-HT4 receptors by single photon emission computed tomography.[16]

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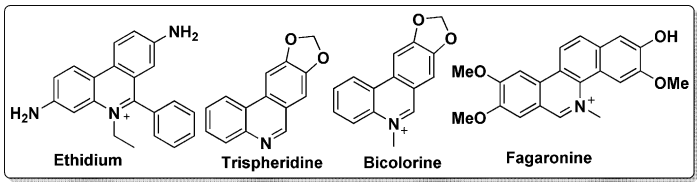


Figure 2. Structures of some DNA intercalating stain containing phenanthridine scaffold.

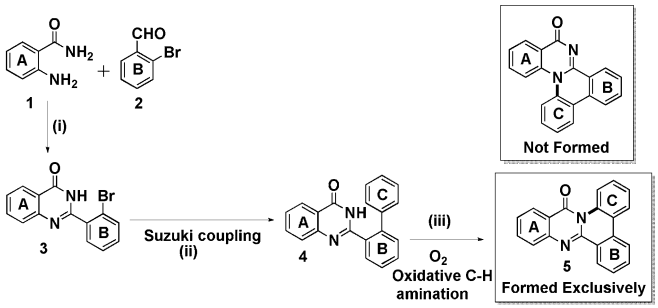
In addition, quinazolinone- and phenanthridine-containing molecular frameworks have been reported in the past as efficient organic electroluminescent materials.[17] Several strategies for an independent construction of quinazolinone or phenanthridine cores are present in the literature,[18] but molecular frameworks containing the quinazolinone and phenanthridine together have not been explored intensely. The research group of Beller and Wu et al.[19] has developed an approach of base-controlled selective synthesis of linear- and angular-fused quinazolinone by a Pd-catalyzed carbonylation and nucleophilic aromatic substitution in sequence. Recently, Alper et al.[20] reported the synthesis of quinazolinone- and pyridine-fused heterocycles by a Pd-catalyzed dearomatizing carbonylation. In the area of discovering new strategies to construct N-fused heterocycles, there is no report for the direct synthesis of quinazolinone- and phenanthridine-fused polyheterocycle by C–H amination. Since the last decade, C–H amination has evolved as a very efficient process due to its atom economy and high bond-formation efficiencies. In comparison with traditional methods for the N-arylation of amine, such as the copper-catalyzed Ullmann/Goldberg method or the palladium-catalyzed Buchwald–Hartwig coupling methods, C–H activation followed by the C–N bond formation provide a complementary direct approach in which no prefunctionalized substrates (like aryl halides, tosylates, and so forth) are required. Therefore, the C–H amination is also a cost-effective and environmentally benign process.

The fusion of quinazolinone ring may occur in two different ways (linear and angular) for two different types of nitrogen atoms that would lead to two regioisomers, and both of the isomers should have some unique pharmacological features. Therefore, a synthetic method, which can provide any one of the two regioisomers exclusively instead of a mixture, is highly desirable.

Results and Discussion

Herein, we report a regioselective and direct synthesis of a specific regioisomer of the quinazolinone- and phenanthridine-fused polycyclic structural framework by an intramolecular C–H amination using an aromatic strained amide nitrogen. However, there are several reports of C–H aminations from acyclic amides,[21] but an amine functionalization of an aromatic C–H bond using a cyclic strained amide nitrogen of an aromatic ring has been a challenging work so far.

In the present study, 2-(2-bromophenyl)quinazolin-4(3H)-ones **3** (precursors to the Suzuki cross-coupling reaction) were synthesized from a condensation followed by the cyclization and oxidation reaction between anthranilamide (**1**) and *o*-bromo benzaldehyde derivatives **2** in 90–95% yield (Scheme 1).[22] Next, in 2-(2-bromophenyl)quinazolin-4(3H)-ones **3**, a new aromatic ring **C** was installed by a well-known Suzuki cross-coupling reaction.[23] Typically compounds **3** were subjected to different arylboronic acids under a palladium catalyst reaction to get the tetra-cyclic compounds **4** in 75–



Reagent & Condition: (i) *p*-TsOH.H_2O (0.1 equiv), PhI$(OAc)_2$ (1.5 equiv), THF, RT; (ii) $PdCl_2$ (5 mol %), $ArB(OH)_2$, (1.5 equiv), K_2CO_3 (2 equiv), EtOH:H_2O (1:1); (iii) $Pd(OAc)_2$ (5 mol%), $Cu(OAc)_2$ (2 equiv), O_2, DMF, 160 °C.

Scheme 1. Synthesis of quinazolinone- and phenanthridine-fused heterocycles by intramolecular C–H amination.

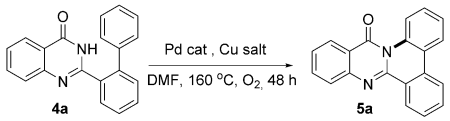
80% yields. The resulted 2-([1,1′-biphenyl]-2-yl)quinazolin-4(3H)-ones **4** were ideally suited for a ring-closing oxidative C–H amination reaction.

The synthesis of fused quinazolinone could proceed in two ways (linear and/or angular) simultaneously. With this in mind, we initially subjected compound **4a** under the oxidative condition using a Pd catalyst and $Cu(OAc)_2$ as co-oxidant in DMSO solvent and heated the reaction mixture at 160 °C for 48 h. Gratifyingly, single regioisomer was formed (from TLC) as confirmed by NMR in a moderate yield (52%). Performing the reaction in toluene as solvent at 120 °C, resulted in no product. Finally, the optimum yield was achieved (74%) by using DMF as solvent.

Without $Cu(OAc)_2$, no product was formed and other co-oxidants like $FeCl_3$, $Ce(SO_4)_2$, DDQ, Ag_2CO_3, $K_2S_2O_8$, or a hypervalent iodine instead of $Cu(OAc)_2$ did not improve the yield of the reaction (Table 1). The reaction was also performed under atmospheric air instead of pure oxygen but the yield was poor (32%). Catalyst screening was performed with various palladium catalysts, and from the study we found $Pd(OAc)_2$ to be the best catalytic agent with 79% yield.

Next, the effect of substituent in the **C** ring was explored (Table 2). We observed that the presence of an electron-donating group in the **C** ring facilitates the reaction and results in high yield, whereas an electron-withdrawing group gives poor yield. The presence of electron-donating methoxy group in the **C** ring at the C_3 position proved to be the best in terms of yield (**5m**, 91%; Table 3), whereas electron-withdrawing effect of the fluoro group produced compound **5e** in only 53%

Table 1. Optimization of the reaction conditions for Pd-catalyzed direct intramolecular amination.[a]



Entry	Catalyst	Oxidant	Co-oxidant	Solvent	Yield [%][b]
1	$PdCl_2$	O_2	$Cu(OAc)_2$	DMSO	52
2	$PdCl_2$	O_2	$Cu(OAc)_2$	toluene	trace
3	$PdCl_2$	O_2	$Cu(OAc)_2$	DMF	74
4	$PdCl_2$	air	$Cu(OAc)_2$	DMF	32
5	$PdCl_2$	O_2	—	DMF	0
6	$PdCl_2$	O_2	Ag_2CO_3	DMF	17
7	$PdCl_2$	O_2	$K_2S_2O_8$	DMF	0
8	$PdCl_2$	O_2	BQ	DMF	0
9	$PdCl_2$	O_2	$Ce(SO_4)_2$	DMF	trace
10	$PdCl_2$	O_2	$FeCl_3$	DMF	trace
11	$PdCl_2$	–	$PhI(OAc)_2$	DMF	trace
12	$Pd(OAc)_2$	O_2	$Cu(OAc)_2$	DMF	79
13	$Pd(acac)_2$	O_2	$Cu(OAc)_2$	DMF	56
14	$[PdCl_2(PPh_3)_2]$	O_2	$Cu(OAc)_2$	DMF	37
15	$[Pd(PPh_3)_4]$	O_2	$Cu(OAc)_2$	DMF	trace

[a] Reaction conditions: **4** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.01 mmol, 5 mol%), $Cu(OAc)_2$ (0.4 mmol, 2 equiv), DMF (3 mL), O_2, 160 °C. [b] Isolated yield.

yield. Interestingly, the presence of a methoxy group in the **B** ring at the C_5 position gave poor yield (**5k** and **5l**). The general molecular framework was confirmed from the crystal structure of compound **5h** (Figure 3).[24]

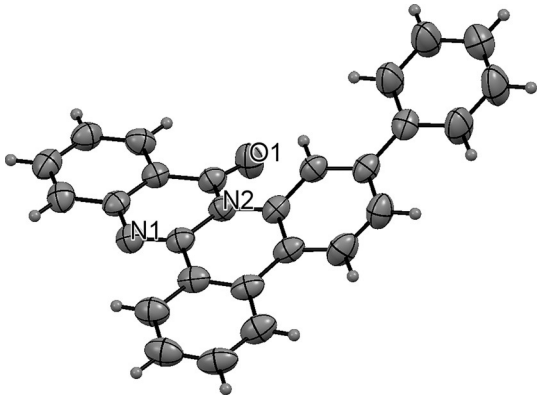
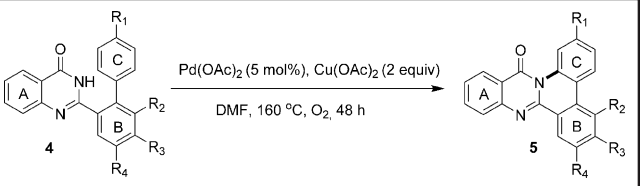
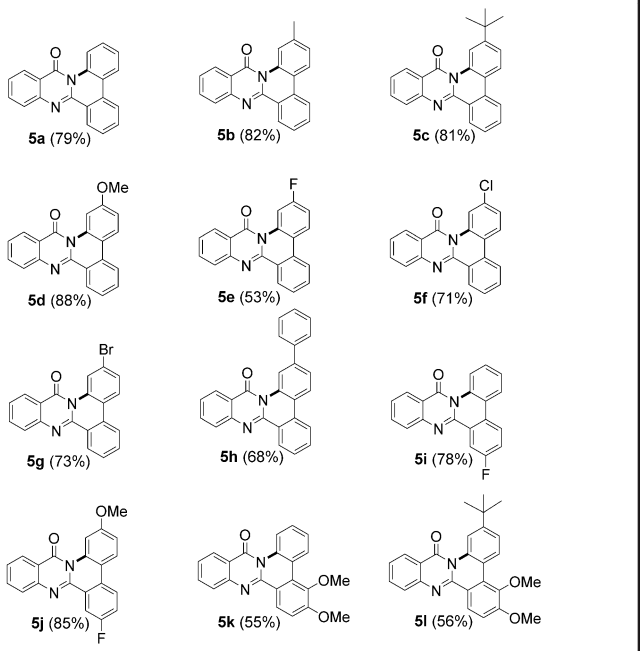


Figure 3. Crystal structure of **5h** (50% thermal ellipsoid).

In the intramolecular amination, the question of regioselectivity arises in the case of substrates in which meta-substituted phenyl boronic acids are used to install the **C** ring. To our delight, at this point also the reaction was very much regioselective, producing only one regioisomer. This could be due to the fact that the substituent at the **C** ring remains away from the amide group, hence minimizing the steric hindrance (Table 3). Due to this steric factor, when the **C** ring was installed by 3,4,5-trimethoxyphenyl boronic acid, there was no transformation in the final amination step (Table 4). Thus, the presence of substitution at 3- and 5-position of the **C** ring inhibits the final

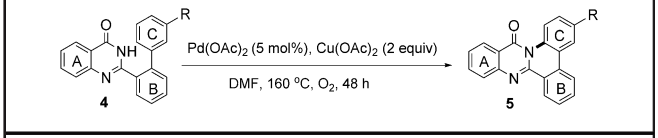
Table 2. Synthesis of 14H-quinazolino[3,2-f]phenanthridin-14-ones by Pd-catalyzed intramolecular C–H amination from 2-([1,1′-biphenyl]-2-yl)-quinazolin-4(3H)-ones.[a]

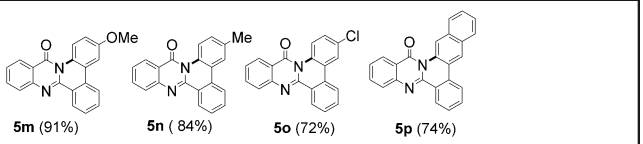




[a] Reaction conditions: **4** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.01 mmol, 5 mol%), $Cu(OAc)_2$ (0.4 mmol, 2 equiv), DMF (3 mL), O_2, 160 °C; isolated yield.

Table 3. Regioselectivity in the **C** ring during final intramolecular C–H Amination.[a]

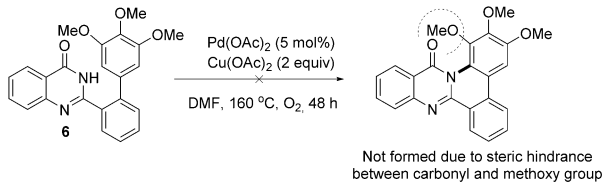




[a] Reaction conditions: **4** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.01 mmol, 5 mol%), $Cu(OAc)_2$ (0.4 mmol, 2 equiv), DMF (3 mL), O_2, 160 °C; isolated yield.

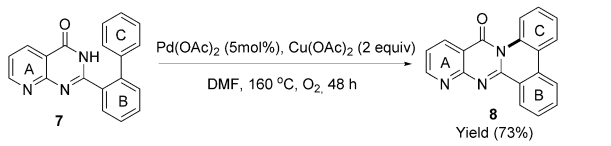
cyclization. However, the presence of electron-withdrawing fluoro group at the **B** ring (**5i** and **5j**; Table 2) does not make any significant difference in the yield. The substrate scope also allows the **A** ring to be a heteroaromatic, such as pyridine, and gratifyingly substrate **7** was cyclized to **8** in 73% yield (Table 5).

Table 4. Investigation of the factor for regioselection in the **C** Ring during amination.[a]



[a] Reaction conditions: **6** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.01 mmol, 5 mol%), $Cu(OAc)_2$ (0.4 mmol, 2 equiv), DMF (3 mL), O_2, 160 °C.

Table 5. Synthesis of 14H-pyrido[2′,3′:4,5]pyrimido[1,2-f]phenanthridin-14-one by Pd-catalyzed intramolecular C–H amination.[a]



[a] Reaction conditions: **7** (0.2 mmol, 1.0 equiv), $Pd(OAc)_2$ (0.01 mmol, 5 mol%), $Cu(OAc)_2$ (0.4 mmol, 2 equiv), DMF (3 mL), O_2, 160 °C; isolated yield.

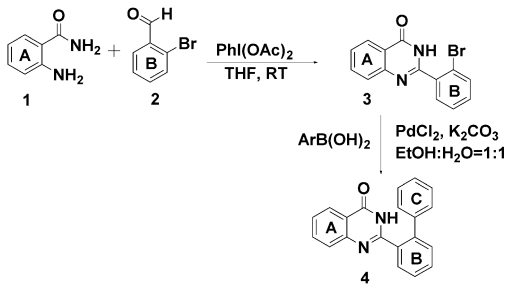
Because a number of nitrogen-containing heterocycles have fluorescent properties and could be used as good fluorophores, we further investigated the photophysical properties of the 14H-quinazolino[3,2-f]phenanthridine-14-one derivatives. The UV/Vis and fluorescence spectra of such compounds were recorded in CH_2Cl_2. All the compounds showed good blue fluorescence upon UV irradiation at 365 nm. It was observed that the compounds containing electron-donating groups (like OMe, CH_3, and so forth) at C2-position of the **C** ring showed good fluorescence intensity due to the extended conjugation (Figure 4).

Conclusion

In summary, we have developed a novel approach to construct quinazolinone- and phenanthridine-fused pentacyclic compounds, which are ubiquitous in the field of medicinal and material science, efficiently by a regioselective palladium-catalyzed C–H bond activation followed by an intramolecular amination of 2-biphenyl-2-yl-3H-quinazolin-4-ones. Detailed studies on elucidation of a mechanism and the use of quinazolinone motif as a new directing group are ongoing in our laboratory.

Experimental Section

Preparation of 2-([1,1′-biphenyl]-2-yl)quinazolin-4(3H)-one (4): First, anthranilamide (5 mmol) and *p*-toluenesulfonic acid monohydrate (5 mol%) were added in THF at room temperature. Then, *o*-bromobenzaldehyde (5.5 mmol) was added slowly while stirring, followed by the addition of iodobenzene diacetate (1.5 equiv), a strong oxidizing agent, portion wise. The reaction was completed after 1 hour, producing **3**, which was subjected to the well-known Suzuki cross-coupling reaction leading to the arylated product **4**.



Preparation of 2-([1,1′-biphenyl]-2-yl) pyrido [2,3-d] pyrimidine-4(3H)-one (7): The reaction was carried out in three steps. In the first step, 2-aminonicotinamide (2 mmol) and *o*-bromobenzaldehyde (2 mmol) were mixed in the presence of catalytic amounts of glacial acetic acid, and the reaction mixture was refluxed overnight. Then, the reaction mixture was neutralized and the cyclized product was washed with cold water and dried. In the second step, the

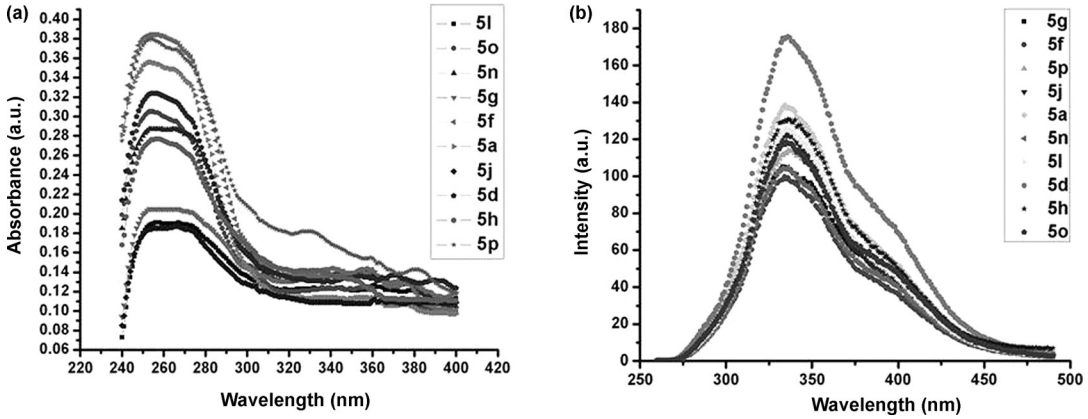
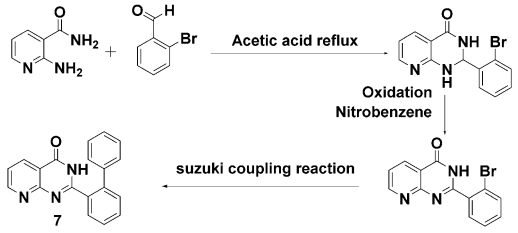
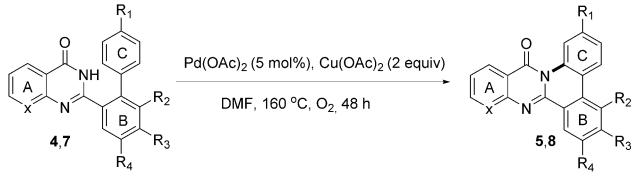


Figure 4. (a) UV/Vis; (b) fluorescence spectra of quinazolinone-fused phenanthridines (5 μM in CH_2Cl_2, $\lambda_{ex} = 280$ nm).

cyclized product was subjected to oxidation by overnight reflux in nitrobenzene solvent. In the final step, a Suzuki cross-coupling reaction was performed with the oxidized product to achieve **7**.



Typical procedure for a Pd-Catalyzed intramolecular C–H amination: To a solution of **4** or **7** (59.6 mg, 0.2 mmol, 1.0 equiv) in DMF (3 mL), $Pd(OAc)_2$ (1.8 mg, 0.01 mmol, 5 mol%) and $Cu(OAc)_2$ (80 mg, 0.4 mmol, 2 equiv) were added in a sealed tube (50 mL) under oxygen atmosphere. The reaction mixture was stirred for 15 min at room temperature and then heated at 160 °C while vigorously stirring for 48 h. The reaction mixture was then cooled to room temperature, diluted with dichloromethane, and filtered through a small pad of celite. The filtrate was concentrated in vacuo and purified by either silica gel or neutral alumina packed flash column chromatography with petroleum ether/ethyl acetate (24:1) as the eluent to afford the desired product **5** or **8**.



14H-quinazolino[3,2-f]phenanthridin-14-one (5a): White solid (79%); m.p. 167–169; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.10 (d, J = 12 Hz, 1H), 8.99 (d, J = 6 Hz, 1H), 8.43 (d, J = 12 Hz, 1H), 8.23 (dd, J_1 = 6 Hz, J_2 = 12 Hz, 2H), 7.82 (d, J = 6 Hz, 2H), 7.72 (t, J = 6 Hz, 1H), 7.59 (t, J = 6 Hz, 1H), 7.53–7.47 ppm (m, 3H), ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.5, 146.0, 145.7, 134.1, 132.6, 131.7, 130.9, 128.1, 127.8, 127.7, 126.9, 126.7, 126.5, 126.0, 125.8, 122.6, 121.7, 121.4, 120.4 ppm; HRMS (EI): *m/z* calcd for $C_{20}H_{12}N_2O$: 296.0950; found: 296.0955; FTIR: $\tilde{\nu}$ = 1687, 1602, 1554, 748 cm^{-1}.

2-methyl-14H-quinazolino[3,2-f]phenanthridin-14-one (5b): White solid (82%); m.p. 146–148 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.97 (d, J = 12 Hz, 1H), 8.91 (s, 1H), 8.43–8.41 (m, 1H), 8.15 (d, J = 6 Hz, 1H), 8.10 (d, J = 6 Hz, 1H), 7.82 –7.81 (m, 2H), 7.70–7.68 (m, 1H), 7.57–7.50 (m, 2H), 7.28 (d, J = 6 Hz, 1H), 2.51 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.6, 146.1, 145.7, 137.9, 134.0, 132.5, 131.7, 131.0, 127.7, 127.6, 127.1, 127.0, 126.5, 126.3, 125.7, 122.5, 121.9, 121.1, 120.4, 120.1, 21.5 ppm; HRMS (EI): *m/z* calcd for $C_{21}H_{14}N_2O$: 310.1106; found: 310.1073; FTIR: $\tilde{\nu}$ = 1686, 1597, 1548, 766 cm^{-1}.

2-tert-butyl-14H-quinazolino[3,2-f]phenanthridin-14-one (5c): White solid (81%); m.p. 152–154 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.22 (s, 1H), 9.02 (d, J = 12 Hz, 1H), 8.47 (d, J = 6 Hz, 1H), 8.23–8.20 (m, 2H), 7.86–7.82 (m, 2H), 7.74–7.72 (m, 1H), 7.59 (t, 1H), 7.56–7.52 (m, 2H), 1.46 ppm (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.7, 151.0, 146.3, 145.7, 134.0, 132.6, 131.7, 131.0, 127.8, 127.7, 127.0, 126.5, 125.7, 123.5, 122.2, 121.2, 120.4, 120.2, 118.9, 34.9, 30.9 ppm; HRMS (EI): *m/z* calcd for $C_{24}H_{20}N_2O$: 352.1576; found: 352.1567; FTIR: $\tilde{\nu}$ = 1680, 1596, 1551, 768 cm^{-1}.

2-methoxy-14H-quinazolino[3,2-f]phenanthridin-14-one (5d): White solid (88%); m.p. 174–176 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.96 (d, J = 12 Hz, 1H), 8.79 (d, J = 6 Hz, 1H), 8.42 (d, J = 6 Hz, 1H), 8.12 (d, J = 6 Hz, 1H), 8.09 (d, J = 12 Hz, 1H),7.84 –7.82 (m, 2H), 7.67 (t, J = 6 Hz, 1H) 7.53–7.50 (m, 2H), 7.07–7.05 (m, 1H), 3.95 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.8, 158.8, 146.3, 145.6, 134.1, 133.9, 131.7, 131.1, 127.8, 127.0, 126.9, 126.5, 125.7, 125.6, 123.6, 120.7, 120.2, 115.9, 114.0, 105.9, 55.2 ppm; HRMS (EI): *m/z* calcd for $C_{21}H_{14}N_2O_2$: 326.1055; found: 326.1064; FTIR: $\tilde{\nu}$ = 1677,1610, 1557, 759 cm^{-1}.

2-fluoro-14H-quinazolino[3,2-f]phenanthridin-14-one (5e): White solid (53%); m.p. 213–215 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.06–9.03 (m, 1H), 9.01 (d, J = 12 Hz, 1H), 8.43 (d, J = 6 Hz, 1H), 8.25–8.23 (m, 1H), 8.15 (d, J = 6 Hz, 1H), 7.86 –7.83 (m, 2H), 7.73 (t, J = 6 Hz, 1H), 7.60 (t, J = 6 Hz, 1H), 7.55–7.53 (m, 1H), 7.26–7.23 ppm (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.5, 162.2, 160.5, 145.8, 145.5, 134.4, 133.8, 133.7, 131.9, 130.3, 128.0, 127.0, 126.6, 126.2, 126.0, 124.2, 121.2, 120.1, 119.0, 113.8, 113.7, 109.3, 109.1 ppm (additional peaks appeared due to the splitting by the fluoro group); HRMS (EI): *m/z* calcd for $C_{20}H_{11}FN_2O$: 314.0833; found: 314.0855; FTIR: $\tilde{\nu}$ = 1682, 1604, 1556, 757 cm^{-1}.

2-chloro-14H-quinazolino[3,2-f]phenanthridin-14-one (5f): White solid (71%); m.p. 199–201 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.24 (s, 1H), 8.98 (d, J = 6 Hz, 1H), 8.42 (d, J = 6 Hz, 1H), 8.15 (t, J = 6 Hz, 2H), 7.86–7.82 (m, 2H), 7.72 (t, J = 6 Hz, 1H), 7.61 (t, J = 6 Hz, 1H), 7.55–7.53 (m, 1H), 7.46 ppm (d, J = 12 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 62.4, 145.5, 145.5, 134.4, 133.6, 133.3, 131.9, 130.0, 128.4, 127.9, 127.0, 126.6, 126.3, 126.1, 123.7, 121.8, 121.3, 121.2, 120.2 ppm; HRMS (EI): *m/z* calcd for $C_{20}H_{11}ClN_2O$: 330.0560; found: 330.0562; FTIR: $\tilde{\nu}$ = 1689, 1599, 1554, 759 cm^{-1}.

2-bromo-14H-quinazolino[3,2-f]phenanthridin-14-one (5g): Grayish White solid (73%); m.p. 180–182 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.35 (s, 1H), 8.92 (d, J = 6 Hz, 1H), 8.40 (d, J = 12 Hz, 1H), 8.09 (d, J = 6 Hz, 1H), 8.03 (d, J = 6 Hz, 1H), 7.82–7.78 (m, 2H), 7.67 (t, J = 6 Hz, 1H), 7.58–7.51 ppm (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.3, 145.4, 134.3, 133.3, 131.8, 130.0, 129.1, 128.4, 127.8, 127.0, 126.6, 126.3, 126.1, 124.6, 123.8, 123.6, 121.6, 121.5, 121.2, 120.1 ppm; HRMS (EI): *m/z* calcd for $C_{20}H_{11}BrN_2O$: 374.0055; found: 374.0043; FTIR: $\tilde{\nu}$ = 1684, 1595, 1549, 759 cm^{-1}.

2-phenyl-14H-quinazolino[3,2-f]phenanthridin-14-one (5h): White solid (68%); m.p. 179–181 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.41 (s, 1H), 9.02 (d, J = 12 Hz, 1H), 8.45 (d, J = 6 Hz, 1H), 8.29 (d, J = 12 Hz, 1H), 8.23 (d, J = 12 Hz, 1H), 7.85–7.83 (m, 2H), 7.77–7.72 (m, 4H), 7.62–7.59 (m, 1H), 7.54–7.49 (m, 3H), 7.43–7.40 ppm (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.7, 146.1, 145.7, 140.4, 139.7, 134.1, 133.0, 131.8, 130.7, 128.5, 128.0, 127.8, 127.4, 127.0, 126.9, 126.7, 126.5, 125.8, 124.7, 123.0, 121.6, 121.4, 120.37, 120.36 ppm; HRMS (EI): *m/z* calcd for $C_{26}H_{16}N_2O$: 372.1263, found: 372.1262; FTIR: $\tilde{\nu}$ = 1678, 1590, 1552, 760 cm^{-1}.

7-fluoro-14H-quinazolino[3,2-f]phenanthridin-14-one (5i): White solid (78%); m.p. 210–212 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.12 (d, J = 12 Hz, 1H), 8.68 (d, J = 6 Hz, 1H), 8.44 (d, J = 12 Hz, 1H), 8.24–8.19 (m, 2H), 7.84 (s, 2H), 7.56–7.44 ppm (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 163.0, 162.4, 161.3, 145.4, 145.0, 134.2, 132.3, 128.9, 128.9, 127.6, 127.4, 127.0, 126.6, 126.2, 123.9, 123.8, 122.5, 122.0, 121.8, 120.5, 120.0, 119.8, 113.5, 113.4 ppm (additional peaks appeared due to the splitting by the fluoro group); HRMS (EI): *m/z*

calcd for $C_{20}H_{11}FN_2O$: 314.0855; found: 314.0844; FTIR: $\tilde{\nu}$ = 1684, 1607, 1554, 753 cm^{-1}.

7-fluoro-2-methoxy-14H-quinazolino[3,2-f]phenanthridin-14-one (5j): White solid (85%); m.p. 226–228 °C; ^1H NMR (600 MHz, $CDCl_3$) δ = 8.77 (d, J = 2.46 Hz, 1H), 8.56–8.54 (m, 1H), 8.38 (d, J = 6 Hz, 1H), 8.01–7.97 (m, 2H), 7.82–7.76 (m, 2H), 7.52–7.49 (m, 1H), 7.35–7.32 (m, 1H), 7.02–7.00 (m, 1H), 3.92 ppm (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.5, 162.2, 160.6, 158.6, 145.2, 145.20, 145.16, 134.1, 133.5, 127.5, 126.9, 126.5, 126.0, 123.3, 123.02, 122.97, 120.2, 119.9, 119.7, 115.0, 114.0, 113.3, 113.2, 105.9, 55.1 ppm) (additional peaks appeared due to the splitting of the fluoro group); HRMS (EI): *m/z* calcd for $C_{21}H_{13}FN_2O_2$: 344.0961; found: 344.0963; FTIR: $\tilde{\nu}$ = 1680, 1613, 1554, 763 cm^{-1}.

5,6-dimethoxy-14H-quinazolino[3,2-f]phenanthridin-14-one (5k): White solid (55%); m.p. 190–192 °C; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.14 (d, J = 9 Hz, 1H), 8.80 (d, J = 6 Hz, 2H), 8.38 (d, J = 9 Hz, 1H), 7.77 (s, 2H), 7.49–7.44 (m, 3H), 7.19 (d, J = 9 Hz, 1H), 4.04 (s, 3H) 3.88 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.7, 156.2, 146.7, 146.6, 145.7, 134.5, 132.6, 128.0, 127.4, 126.7, 125.8, 125.5, 125.1, 122.8, 121.9, 121.6, 120.5, 112.5, 60.6, 56.2 ppm; HRMS (EI): *m/z* calcd for $C_{22}H_{16}N_2O_3$: 356.1161; found: 356.1167; FTIR: $\tilde{\nu}$ = 1671, 1594, 1553, 755 cm^{-1}.

2-tert-butyl-5,6-dimethoxy-14H-quinazolino[3,2-f]phenanthridin-14-one (5L): White solid (56%); m.p. 175–177 °C; ^1H NMR (600 MHz, $CDCl_3$) δ = 9.08 (d, J = 12 Hz, 1H), 8.90 (d, J = 1.92 Hz, 1H), 8.81 (d, J = 6 Hz, 1H), 8.44 (d, J = 12 Hz, 1H), 7.82–7.78 (m, 2H), 7.53–7.47 (m, 2H), 7.19 (d, J = 6 Hz, 1H), 4.05 (s, 3H), 3.90 (s, 3H), 1.44 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.4, 155.9, 150.8, 146.6, 146.2, 145.0, 134.0, 132.1, 127.0, 126.5, 126.2, 125.2, 124.7, 123.7, 121.3, 120.2, 119.7, 118.3, 111.7, 60.1, 55.7, 34.7, 30.8 ppm; HRMS (EI): *m/z* calcd for $C_{26}H_{24}N_2O_3$: 412.1787; found: 412.1780; FTIR: $\tilde{\nu}$ = 1680, 1586, 1547, 768 cm^{-1}.

3-methoxy-14H-quinazolino[3,2-f]phenanthridin-14-one (5m): White solid (91%); m.p. 171–172 °C; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.13 (d, J = 9 Hz, 1H), 9.03 (d, J = 9 Hz, 1H), 8.42 (d, J = 9 Hz, 1H), 8.17 (d, J = 9 Hz, 1H) 7.83 (s, 2H), 7.75–7.69 (m, 2H), 7.61 (t, J = 6 Hz, 1H), 7.53–7.48 (m, 1H), 7.10–7.06 (m, 1H), 3.96 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.8,157.5, 146.2, 146.1, 134.4, 132.1, 131.2, 128.7, 128.4, 127.5, 127.3, 127.0, 126.9, 126.1, 124.6, 123.8, 121.9, 120.7, 114.2, 107.1 ppm; HRMS (EI): *m/z* calcd for $C_{21}H_{14}N_2O_2$: 326.1055; found: 326.1050; FTIR: $\tilde{\nu}$ = 1690, 1617, 1552, 754 cm^{-1}.

3-methyl-14H-quinazolino[3,2-f]phenanthridin-14-one (5n): White solid (84%); m.p. 150–151 °C; ^1H NMR (600 MHz, $CDCl_3$) δ = 9.01 −8.99 (m, 2H), 8.42 (d, J = 6 Hz, 1H), 8.20 (d, J = 12 Hz, 1H), 8.02 (s, 1H), 7.82–7.81 (m, 2H), 7.71–7.69 (m, 1H), 7.59–7.56 (m, 1H), 7.52–7.50 (m, 1H), 7.32–7.30 (m, 1H), 2.50 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.5,145.9, 145.7, 135.7, 134.0, 131.6, 130.9, 130.4, 128.6, 127.9, 127.8, 126.9, 126.8, 126.4, 125.7, 122.7, 122.4, 121.5, 121.3, 120.3, 20.8 ppm; HRMS (EI) *m/z* calcd for $C_{21}H_{14}N_2O$: 310.1092; found: 310.1081; FTIR: $\tilde{\nu}$ = 1687, 1598, 1548, 766 cm^{-1}.

3-chloro-14H-quinazolino[3,2-f]phenanthridin-14-one(5O): White solid (72%); m.p. 209–210 °C; ^1H NMR (600 MHz, $CDCl_3$) δ = 9.10 (d, J = 12 Hz, 1H), 8.96 (d, J = 6 Hz, 1H), 8.39 (d, J = 6 Hz, 1H), 8.15 (s, 1H), 8.11 (d, J = 6 Hz, 1H), 7.84–7.80 (m, 2H), 7.71 (t, J = 6 Hz, 1H), 7.61 (t, J = 6 Hz, 1H), 7.52 (t, J = 6 Hz, 1H), 7.45–7.43 ppm (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 162.3,145.5, 145.4, 134.3, 131.9, 131.6, 131.1, 129.6, 128.7, 127.9, 127.5, 127.0, 126.9, 126.6, 126.0, 124.3, 123.2, 122.3, 121.4, 120.2 ppm; HRMS (EI): *m/z* calcd for $C_{20}H_{11}ClN_2O$: 330.0560; found: 330.0570; FTIR: $\tilde{\nu}$ = 1681, 1620, 1551, 759 cm^{-1}.

17H-benzo[b]quinazolino[3,2-f]phenanthridin-17-one (5p): White solid (74%); m.p. 204–206 °C; ^1H NMR (600 MHz, $CDCl_3$) δ = 9.60 (s, 1H), 8.91 (d, J = 6 Hz, 1H), 8.54 (s, 1H), 8.43 (d, J = 6 Hz, 1H), 8.25 (d, J = 12 Hz, 1H), 7.91 (d, J = 12 Hz, 1H), 7.86 (d, J = 6 Hz, 1H), 7.83–7.79 (m, 2H), 7.65 (t, J = 6 Hz, 1H); 7.54–7.49 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.7, 145.9, 145.4, 134.0, 132.0, 131.7, 131.0, 130.5, 129.9, 128.1, 128.1, 127.9, 127.0, 126.6, 126.6, 126.5, 126.2, 126.0, 121.7, 121.7, 121.5, 120.6, 120.1 ppm; HRMS (EI): *m/z* calcd for $C_{24}H_{14}N_2O$: 346.1106; found: 346.1089; FTIR: $\tilde{\nu}$ = 1684, 1591, 1551, 766 cm^{-1}.

14H-pyrido[2′,3′:4,5]pyrimido[1,2-f]phenanthridin-14-one (8): White solid (73%); m.p. 175–177 °C; ^1H NMR (300 MHz, $CDCl_3$) δ = 9.22 (d, J = 9 Hz, 1H), 9.12–9.06 (m, 2H), 8.76 (d, J = 9 Hz, 1H), 8.35–8.28 (m, 2H), 7.81 (t, J = 6 Hz, 1H), 7.69–7.64 (m, 1H), 7.57–7.55 (m, 2H), 7.50–7.46 ppm (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.4, 156.7, 156.0, 149.6, 137.2, 133.2, 132.6, 131.8, 129.3, 128.8, 128.4, 127.0, 126.6, 123.3, 123.2, 122.0, 121.8, 121.6 ppm; HRMS (EI): *m/z* calcd for $C_{19}H_{11}N_3O$: 297.0902; found: 297.0895; FTIR: $\tilde{\nu}$ = 1685, 1602, 1550, 769 cm^{-1}.

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[24] CCDC 1419906 (**5h**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre. See the Supporting Information for details.

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