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ARTICLE

One-Pot Sequential Reaction to 2-Substituted-Phenanthridinones from *N*–Methoxybenzamides

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Dongdong Liang,[a] Deanna Sersen,[a] Chao Yang,[c] Jeffrey R. Deschamps,[b] Gregory H. Imler,[b] Chao Jiang,[c,*] and Fengtian Xue[a,*]

Sequential use of hypervalence iodine reagent leads to the one-pot synthesis of 2-bromo/chloro-phenanthridinones via an amidations of arene followed by a regioselective halogenation reaction. These consecutive C-H functionalization reactions can be used efficiently to construct 2-substituted-phenanthridinones at room temperature with good to high yields. Application of the current method is highlighted by the concise synthesis of natural product PJ34.

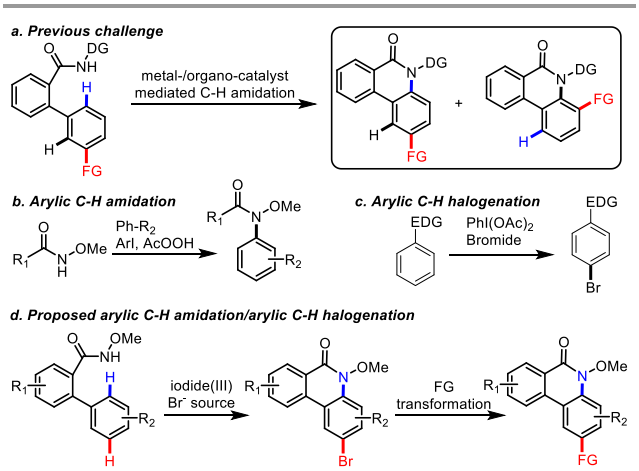
Introduction

Atom-economy sequential reactions using readily available catalyst/reagent are desirable in organic chemistry. Metals such as Pd(II),[1] Cu(I),[2] and Fe(II),[3] have been successfully used in catalyzing sequential reactions. Organocatalysts, on the other hand, have not found similar applications. Herein we report a hypervalent iodine mediated one-pot process involving a C-H amidation and selective halogenation in a sequential matter, leading to the synthesis of 2-substituted-phenanthridinones.

Phenanthridinones is a privileged scaffold for biologically active compounds. Phenanthridinone-based natural product PJ34, an inhibitor of the human poly(ADP-ribose) polymerase 1, is used as a cytoprotective[4] and neuroprotective agent.[5] The [^{11}C]PJ34 is a novel radiotracer, to elucidate the role of PARP1 in necrosis.[6] Crinasiadine, another phenanthridinone-based natural product, shows promising antimicrobial and antifungal activities.[7] In addition, phenanthridinone derivatives have been developed as the HIV integrase inhibitors for the treatment of HIV infections.[8] Functionalized phenanthridinones have be reported to limit the cytotoxicity of doxorubicin.[9]

Syntheses to phenanthridinones are known.[10] For example, Wang,[10a] Cheng,[10b-d] and others[10e-f] used Pd(II)- or Rh(III)-catalyzed C-H amidation to yield phenanthridinones. In the presence of metal catalyst oxidative CO insertion has been used to prepare phenanthridinones.[10g-j] However few organocatalyst mediated synthesis of phenanthridinones have been reported.[11] In the development of novel inhibitors of the transcriptional repressor protein BCL6, we are interested in a practical method to 2-functionalized phenanthridinones.[12] Although target compounds can be obtained by following reported methods starting from functionalized *N*-methoxybenzamides (Scheme 1a), these strategies inevitably led to a mixture of regioisomers that are challenging to separate.

An appealing alternative is via sequential and selective C-H functionalization. Antonchick pioneered direct arylic C-H amidation using hypervalent iodine (Scheme 1b).[13] Experimental evidence also showed that in the presence of a hypervalent iodine, electron rich arenes can undergo halogenation with proper halogen sources, to yield 1,4-disubstituted arenes (Scheme 1c).[14] Exploiting these parallel conditions, we speculated that a one-pot sequential hypervalent iodine-mediated reaction would be possible with unfunctionalized substrate (Scheme 1d), to facilitate an efficient route to functionalized phenanthridinones.



Scheme 1. Routes to Functionalized Phenanthridinones

Results and discussion

We initiated our studies using *N*-methoxy-[1,1'-biphenyl]-2-carboxamide **1a** as the starting material to build 2-bromo-

[a] Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, 20 Penn Street, Baltimore, Maryland 21201, United States Phone: 410-706-8521. Email: fxue@rx.umaryland.edu
[b] Naval Research Laboratory, Code 6930, 4555 Overlook Ave., Washington, DC 20375, United States
[c] Department of Pharmaceutical Engineering, School of Chemical Engineering, Nanjing University of Science and Technology, Nanjing, Jiangsu 210094, China, Phone: 86-18601406179. Email: chaojiang@njust.edu.cn
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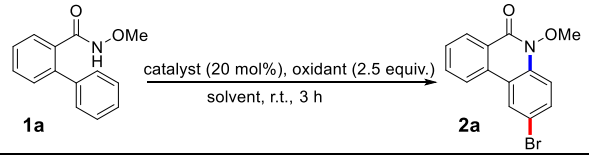
phenanthridinone **2a** using PhI as a catalyst, AcOOH as an oxidant, and TBAB as a bromide source. Different solvents including HFIP, TFE, CH_3CN, DCM, DMSO, DMF, and H_2O were screened (entries 1-7), and the results indicated that HFIP was the best. When *m*CPBA was used to replace AcOOH, slightly decreased yields were obtained (entry 8). Other bromide sources including NH_4Br (entry 9), LiBr (entry 10), NaBr (entry 11), and KBr (entry 12) all resulted in decreased yields. Direct employment of hypervalent iodine reagents PIDA and PhIO gave slightly higher yields (entries 13-14). To the best of our knowledge, our results represent the first PhI-catalyzed synthesis of 2-bromo-phenanthridinone starting from substrate **1a**.

Table 1. Optimization of Conditions for Compound **2a**[a]



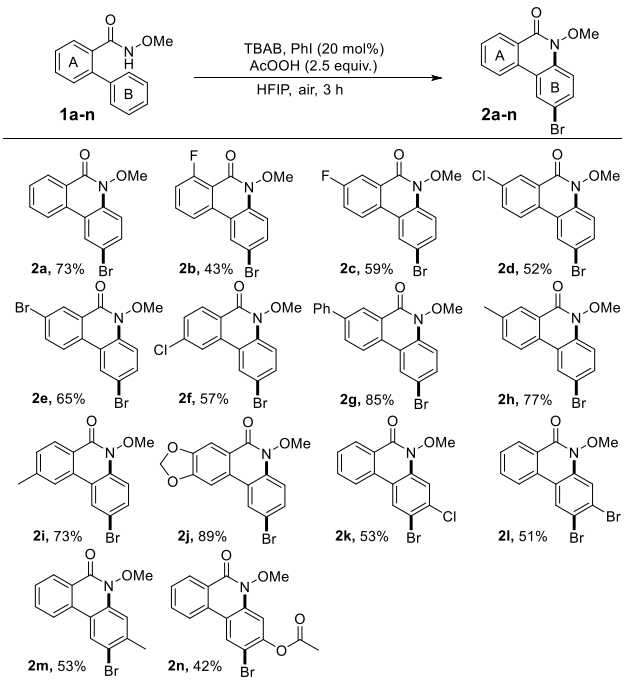
1a 2a

Entry	Cat.	Oxidant	Br source	Solvent	Yield[b] (%)
1	PhI	AcOOH	TBAB	HFIP	73
2	PhI	AcOOH	TBAB	TFE	17
3	PhI	AcOOH	TBAB	CH_3CN	42
4	PhI	AcOOH	TBAB	DCM	42
5	PhI	AcOOH	TBAB	DMSO	33
6	PhI	AcOOH	TBAB	DMF	20
7	PhI	AcOOH	TBAB	H_2O	21
8	PhI	*m*CPBA	TBAB	HFIP	62
9	PhI	AcOOH	NH_4Br	HFIP	42
10	PhI	AcOOH	LiBr	HFIP	67
11	PhI	AcOOH	NaBr	HFIP	63
12	PhI	AcOOH	KBr	HFIP	70
13	-	PIDA	TBAB	HFIP	81
14	-	PhIO	TBAB	HFIP	79

[a]A mixture of substrate **1a** (0.25 mmol), bromide source (1.2 equiv.), PhI (20 mol %), oxidant (2.5 equiv.) in 1.0 mL solvent was stirred at room temperature for 3 h. TBAB = tetrabutylammonium bromide, HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol, TFE = 2,2,2-trifluoroethanol, CH_3CN = acetonitrile, DCM = dichloromethane, DMSO = dimethyl sulfoxide, DMF = dimethylformamide, *m*CPBA = meta-chloroperoxybenzoic acid, PIDA = (diacetoxyiodo)benzene, PhIO = iodosobenzene. [b]Isolated yields.

With the optimized conditions in hand, we next explored the substrate tolerance of the reaction using other *N*-methoxybenzamide (Table 2). Moderate yields were observed for substrates that contain halogen substituents on the A-ring (**2b-f**). When a phenyl group was present on the A-ring, the corresponding product **2g** was formed in high yields. We were pleased to find that the bromination only took place at the para-position of newly formed C-N bond. When methylated substrates were used, slightly increased yields of compounds **2h-i** were obtained. The substrate containing the electron-donating 1,3-dioxole group reacted smoothly to generate compound **2j** in excellent yields. Compound **2j** represents the core structure of natural product crinasiadine. Substrates bearing various substitutions on the B-ring were also studied. In general products with two functional groups on the B-ring could be constructed with moderate yields (**2k-n**), likely due to the increased steric hindrance of the *N*-methoxybenzamide starting material. For the reactions that gave relatively low yields (< 60%), we repeated them and used PIDA directly instead of the catalytic system. For most cases a small improvement in yields were obtained (Scheme S1).

Table 2. Scope of *N*-Methoxybenzamides[a,b]



[a]Reaction conditions: substrate 1 (0.25 mmol), TBAB (1.2 equiv.) PhI (20 mol %), AcOOH (2.5 equiv.) in 1.0 mL solvent was stirred at room temperature for 3 h. [b]Isolated yields.

To further extend the scope of the method, we studied the corresponding chlorination reactions using TBAC as a chloride source (Table 3). When compound **1a** was used as a substrate under the optimized conditions, the corresponding 2-chloro-phenanthridinone **3a** was achieved in high yields. Similar high yields were obtained in reactions using PIDA. Other functional groups such as Me, Cl, Br also were well-tolerated in stoichiometric PIDA. High yields corresponding products were produced successfully (**3b-3f**). While with the catalytic conditions, a mixture of the inseparable chlorinated and unchlorinated phenanthridinones was obtained (supporting information). The chemical structure of compound **3f** was confirmed by X-ray crystallography.

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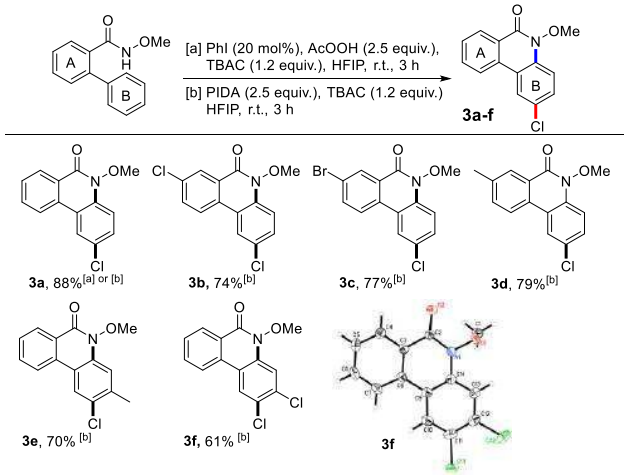
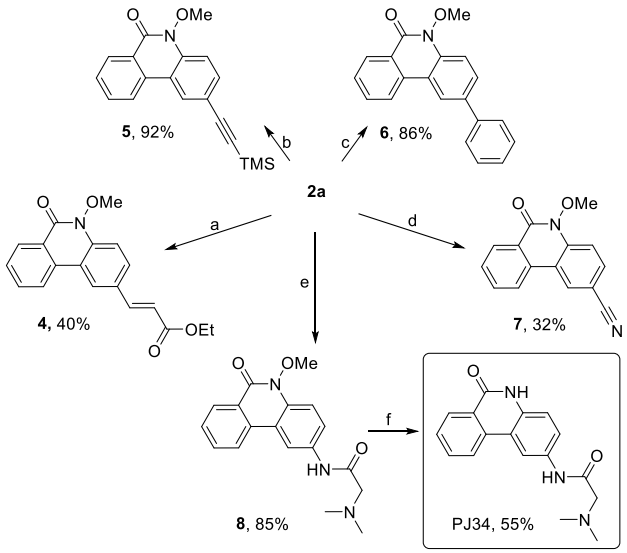
Table 3. Scope of Chlorination[a,b]



[a]Reaction conditions: **1** (0.25 mmol), TBAC (1.2 equiv.), PIDA (2.5 equiv.) in 1.0 mL HFIP was stirred at room temperature for 12 h. [b]Isolated yields TBAC = tetrabutylammonium chloride.

2-Bromo-phenanthridinones represent key intermediates to other 2-functionalized phenanthridinones (Scheme 2). Heck reaction between compound **2a** and ethyl acrylate gave compound **4** in modest yields. Sonogashira coupling of **2a** with trimethylsilylacetylene using $Pd(PPh_3)_2Cl_2$ in the present of CuI afforded the arylethynylene **5** in high yields. When treated with phenylboronic acid, compound **2a** reacted smoothly to give 5-methoxy-2-phenylphenanthridin-6(5*H*)-one **6** in good yields. Treatment of **2a** with CuCN upon heating yielded 2-cyano-phenanthridinones **7** in modest yields. Finally, Pd-catalyzed amidation of compound **2a** with 2-(dimethylamino)acetamide generated compound **8** in high yields, which was further deprotected to yield PJ34 in good yields.[10(h),15]

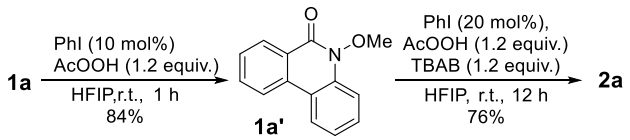


Scheme 2. Derivatization of Compound **2a**. Reaction conditions: a) ethyl acrylate, $Pd(OAc)_2$, PPh_3, K_2CO_3, TBAC, DMF, 120 °C, 40%; b) trimethylsilylacetylene, $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, 80 °C, 92%; c) phenylboronic acid, $Pd(PPh_3)_2Cl_2$, K_2CO_3, dioxane, H_2O, 100 °C, 86%; d) CuCN, L-proline, DMF, 120 °C, 32%; e) 2-(dimethylamino)acetamide, $Pd_2(dba)_3$, Xantphos, Cs_2CO_3, dioxane, 100 °C, 85%; f) NaOH, DMF, 120 °C, 55%.

Next, we expanded the method to construct other heterocycles (Scheme 3). Under our optimized conditions using PIDA, protected [1,1'-biphenyl]-2-amine **9** was cyclized to give compound **10** in modest yields.[16] When *N*-phenylpyridin-2-amine **11** was used, the cross-dehydrogenative coupling product 8-bromobenzo[4,5]imidazo[1,2-*a*]pyridine **12** was generated in modest yields.[17]

Scheme 3. Construction of Other Heterocycle

To gain insight into the mechanism of the sequential reaction, substrate **1a** was treated with AcOOH in the presence of TBAB. No obvious reaction was detected in 12 h. This result supported the important role of the in situ generated hypervalence iodine reagent in the reactions. Results from NMR studies indicated the formation of PIDA when mixing PhI with AcOOH in the presence of TBAB (Figure S1),[14g] which again, supported the key role of hypervalence iodine in the sequential reaction. Reaction of substrate **1a** with PhI (10 mol%) and AcOOH (1.2 equiv.) yielded phenanthridinone **1a'** in good yields (Scheme 4). When compound **1a'** was submitted to our optimal conditions, as expected, phenanthridinone **2a** was isolated as the only product in good yields. This result is in consistent with our hypothesis that the sequential reaction is through the intermediate **1a'**. We also performed a reaction of **1a** with decreased amount of AcOOH (1.2 equiv.), and the result showed the formation of **2a** as the only new product in 36% yield, along with the recovery of starting material **1a** in 56%. This result indicated that the first C-H amidation reaction was the slow step comparing to the bromination step.



Scheme 4. Sequential Generation of Compound **2a**

Based on the results above, a possible mechanism is proposed for the formation of product **2a** under the PhI-catalyzed conditions (Scheme 5). Methoxybenzamide **1a** reacts with the hypervalence iodine reagent that is generated from AcOOH oxidation of PhI, to give intermediate **A.** Electrophilic attack of this intermediate by B-ring provides **B**. Fast deprotonation of intermediate **B** leads to compound **1a'**. The second equivalence of AcOOH generated hypervalence iodine

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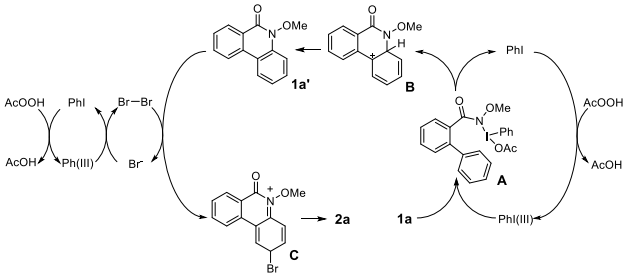
reagent reacts with the bromide source in-situ to generate Br_2. Electrophilic aromatic substitution of compound **1a'** with Br_2 generates the final product **2a** via intermediate **C**.



Scheme 5. Proposed Mechanism for the Formation of **2a**

Conclusions

In summary, we disclose a one-pot sequential hypervalence iodine-mediated amindation/bromination reaction to furnish 2-substituted-phenanthridinones. Using our optimized conditions employing PhI as a catalyst, AcOOH as an oxidant, and TBAB as a bromide source, the reaction goes smoothly at room temperature to yield a wide range of 2-bromo-phenanthridinones in good yields. By switching to a chloride source TBAC in the presence of PIDA and AcOOH, analogs of 2-chloro-phenanthridinones were also obtained in good efficiency. The resulting 2-bromo-phenanthridinones provide a key intermediate for the synthesis of 2-functionalized phenanthridinones, which is highlighted by the concise synthesis of natural product PJ34. Similar reaction conditions can be used to the construction of other heterocyclic systems. The anti-lymphoma activities of the synthesized 2-substituted-phenanthridinones are currently undergoing.

Acknowledgements

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Experimental section

General Considerations

All reagents were purchased without further purification unless otherwise noted. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica gel plates (GF254). Visualization of the developed plates was performed under UV light (254 nm). Flash column chromatography was performed on silica gel (200-300 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA 400 MHz NMR spectrometer at 25 °C. Chemical shifts (δ) are reported in ppm referenced to an internal tetramethylsilane standard, or the DMSO-d_6 residual peak (δ 2.50) for ^{1}H NMR. Chemical shifts of ^{13}C NMR are reported relative to $CDCl_3$ (δ 77.0) or DMSO-d_6 (δ 39.5). The following abbreviations were used to describe peak splitting patterns when appropriate: br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, J values were reported in Hertz unit (Hz). High-resolution mass spectra (HRMS) were obtained on a JEOL AccuTOF with ESI/APCI ion sources coupled to an Agilent 1100 HPLC system.

General Procedure for the Synthesis of Compounds 1a–n.

A mixture of substituted 2-halogenated methyl benzoate (2 mmol), arylboronic acid (3 mmol, 1.5 equiv), $Pd(PPh_3)_2Cl_2$ (0.08 mmol, 0.04 equiv, 56 mg) and potassium carbonate (6 mmol, 3 equiv, 828 mg) in dioxone/H_2O (6 mL / 2 mL) was stirred at 100 °C under argon atmosphere until the starting material was completely consumed (typically 20 h). The reaction mixture was diluted with brine (25 mL). The mixture was then extracted with EtOAc (25 mL × 2), and the combined organic layers were dried over Na_2SO_4. The concentrated crude product was purified by column chromatography to afford substituted methyl [1,1'-biphenyl]-2-carboxylate, which was used directly in the next step.

To a solution of substituted methyl [1,1'-biphenyl]-2-carboxylate in EtOH/H_2O (9 mL, 1:2 (v/v)) was added potassium hydroxide (336 mg, 6 mmol). The resulting mixture was heated under reflux until TLC indicated total consumption of the substrate. The solvent was removed under vacuum, and the resulting residue was dissolved into water (20 mL). To the aqueous solution was added HCl (2 M) until no more precipitate was formed. The mixture was extracted with EtOAc (25 mL × 3), and the combined organic layer was dried with Na_2SO_4. The solvent was removed by rotary evaporation, and the resulting solid was dissolved in DCM (10 mL). To the solution was added 4-dimethylaminopyridine (DMAP) (366 mg, 3 mmol) and methoxylamine hydrochloride (166 mg, 2 mmol) in one portion, followed by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI) (573 mg, 3 mmol). The reaction mixture was allowed to stir at room temperature until TLC indicated completion of the reaction. Saturated aqueous $NaHCO_3$ (10 mL) was added to the reaction mixture. The mixture was extracted with EtOAc (25 mL × 3), and the combined organic layers were dried using Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by silica gel column chromatography using EtOAc/hexanes to give substrates **1a–n**.

N-Methoxy-[1,1'-biphenyl]-2-carboxamide (1a).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (br s, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.43-7.38 (m, 7H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 139.9, 139.6, 132.2, 130.8, 130.1, 129.2, 128.8, 128.7, 128.1, 127.7, 127.2, 64.0.

3-Fluoro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1b).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (br s, 1H), 7.43-7.37 (m, 6H), 7.20 (d, J = 7.6 Hz, 1H), 7.12 (t, J = 8.8 Hz, 1H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 160.0 (J = 250 Hz), 142.5, 138.3, 131.6, (J = 8.9 Hz), 130.8, 128.7, 128.5, 128.3, 125.5, 114.7 (J = 20.9 Hz), 64.2.

4-Fluoro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1c).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (br s, 1H), 7.42-7.35 (m, 7H), 7.25-7.20 (m, 1H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 163.1, 138.6, 136.0, 133.8, 132.0, 131.9, 128.9, 128.7, 128.2, 118.0, 117.8, 116.2, 116.0, 64.0.

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4-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1d).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (br, 1H), 7.67 (s, 1H), 7.50-7.39 (m, 6H), 7.33 (d, J = 7.6 Hz, 1H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 138.3, 133.9, 133.6, 131.5, 130.9, 129.2, 128.9, 128.6, 128.4, 64.0.

4-Bromo-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1e).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (br s, 1H), 7.79 (s, 1H), 7.63 (d, J = 7.2 Hz, 1H), 7.42-7.39 (m, 5H), 7.26 (m, 1H), 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 138.8, 138.4, 133.8, 132.0, 131.7, 128.9, 128.5, 121.8, 64.0.

5-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1f).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69-7.63 (m, 2H), 7.46-7.40 (m, 7H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 141.6, 138.3, 136.7, 130.7, 130.0, 128.9, 128.6, 128.5, 127.8, 64.0.

N-Methoxy-[1,1':4',1''-terphenyl]-2'-carboxamide (1g).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (br s, 1H), 7.75 (d, J = 7.6 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.48-7.39 (m, 9H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 140.7, 139.5, 139.2, 138.6, 132.6, 130.6, 129.3, 128.94, 128.86, 128.7, 128.2, 127.9, 127.1, 64.0.

N-Methoxy-4-methyl-[1,1'-biphenyl]-2-carboxamide (1h).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (br s, 1H), 7.50 (s, 1H), 7.45-7.38 (m, 5H), 7.34-7.29(m, 2H), 3.53 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 139.5, 137.8, 137.0, 131.9, 131.6, 130.0, 129.7, 128.8, 128.7, 127.9, 63.9, 20.9.

N-methoxy-5-methyl-[1,1'-biphenyl]-2-carboxamide (1i).[18] ^{1}H NMR (400 MHz, CDCl3) δ 7.61 (d, J = 7.6 Hz, 1H), 7.46-7.40 (m, 5H), 7.25 (d, J = 8.0 Hz, 1H), 7.19 (s, 1H), 3.54 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 141.0, 139.9, 139.8, 130.7, 129.3, 128.71, 128.66,128.4, 128.0, 63.9, 21.4.

N-Methoxy-6-phenylbenzo[d][1,3]dioxole-5-carboxamide (1j).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (br s, 1H), 7.42-7.35 (m, 5H), 7.14 (s, 1H), 6.80 (s, 1H), 6.04 (s, 2H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.9, 149.6, 147.3, 139.5, 135.0, 128.9, 128.7, 128.1, 125.8, 109.9, 109.2, 101.9, 63.8.

4'-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1k).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (br s, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.44-7.34 (m, 6H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 138.8, 138.0, 134.2, 132.2, 130.9, 130.03, 129.95, 129.0, 128.9, 127.9, 64.1.

4'-Bromo-N-methoxy-[1,1'-biphenyl]-2-carboxamide (1l).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (br s, 1H), 7.58-7.50 (m, 4H), 7.42 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 8.4 Hz, 2H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 138.8, 138.4, 132.2, 131.8, 130.9, 130.3, 130.0, 129.0, 127.0, 122.4, 64.0.

N-Methoxy-4'-methyl-[1,1'-biphenyl]-2-carboxamide (1m).[18] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (br s, 1H), 7.67 (d, J = 6.8 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.43-7.31 (m, 4H), 7.24 (d, J = 7.6 Hz, 2H), 3.58 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 140.0, 137.8, 136.6, 132.1, 130.7, 130.1, 129.4, 129.1, 128.5, 127.4, 63.8, 21.2.

2'-(Methoxycarbamoyl)-[1,1'-biphenyl]-4-yl acetate (1n). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.61 (d, J = 6.8 Hz, 1H), 7.50 (d, J = 7.2 Hz, 1H), 7.43-7.37 (m, 4H), 7.14 (d, J = 7.2 Hz, 2H), 3.54 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 167.2, 150.5, 139.0, 137.2, 132.4, 130.8, 130.0, 129.7, 129.1, 127.8, 121.9, 64.0, 21.1.

General Procedure for Bromination.

Method A: To a solution of *N*-methoxy-[1,1'-biphenyl]- 2-carboxamide (0.25 mmol, 1 equiv) and tetrabutyl ammonium bromide (TBAB) (97 mg, 0.3 mmol, 1.2 equiv) in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.0 mL) was added PhI (5.6 µL, 0.05 mmol, 20 mol%) and peroxyacetic acid (2.5 equiv) (32 wt.% in dilute acetic acid, 131 µL, 0.625 mmol, 2.5 equiv) or iodosobenzene diacetate (PIDA) (201 mg, 0.625 mmol, 2.5 equiv) at 25 ºC under air. The resulting mixture was allowed to stir at 25 °C for an additional 3 h. The reaction was monitored using TLC until the starting material was completely consumed. The reaction mixture was diluted with EtOAc (20 mL) and washed with brine (20 mL). The organic layer was dried over Na_2SO_4, and concentrated under vacuum. The resulting crude product was purified by column chromatography (hexane/EtOAc) to give the desired products 2a-n.

To improve yields of the reactions that gave relatively low yields (< 60%), we repeated them and used PIDA directly instead of the catalytic system. For most of cases a slightly higher yields were obtained as follows.

Method B: To a solution of *N*-methoxy-[1,1'-biphenyl]- 2-carboxamide (0.25 mmol, 1 equiv) and tetrabutyl ammonium bromide (TBAB) (97 mg, 0.3 mmol, 1.2 equiv) in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.0 mL) iodosobenzene diacetate (PIDA) (201 mg, 0.625 mmol, 2.5 equiv) at 25 °C under air. The resulting mixture was allowed to stir at 25 °C for an additional 3 h. The reaction was monitored using TLC until the starting material was completely consumed. The reaction mixture was diluted with EtOAc (20 mL) and washed with brine (20 mL). The organic layer was dried over Na_2SO_4, and concentrated under vacuum. The resulting crude product was purified by column chromatography (hexane/EtOAc) to give the desired products **2a-d**, **2f**, **2h**, **2k-m** (see supporting information Scheme S1).

2-Bromo-5-methoxyphenanthridin-6(5H)-one (2a). White solid, method A: 55 mg, 73% yield; method B: 61 mg, 81% yield, mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, J = 8.8 Hz, 1H), 8.38 (s, 1H), 8.22 (d, J = 8.4 Hz, 1H), 7.81 (t, J = 8.0 Hz, 1H), 7.69-7.63 (m, 2H), 7.56 (d, J = 9.2 Hz, 1H), 4.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 134.8, 132.9, 132.7, 131.7, 128.8, 128.6, 126.5, 126.0, 122.0, 120.2, 116.3, 114.4, 62.8; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}BrNO_2$ $[M+H]^+$ 303.9968, found 303.9983.

2-Bromo-7-fluoro-5-methoxyphenanthridin-6(5H)-one (2b). White solid, method A: 35 mg, 43% yield; method B: 49 mg, 61% yield, mp 188-190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.01 (d, J = 8.8 Hz, 1H), 7.77-7.67 (m, 2H), 7.52 (d, J = 8.4 Hz, 1H), 7.30 (t, J = 8.8 Hz, 1H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (J = 264.9 Hz), 154.2, 135.2, 134.4, 133.8 (J = 10.4 Hz), 133.5, 126.5, 119.1, 117.9 (J = 4.5 Hz), 116.32 (J = 20.8 Hz), 116.31, 115.5, 114.3, 62.8; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}BrFNO_2$ $[M+H]^+$ 321.9873, found 321.9887.

2-Bromo-8-fluoro-5-methoxyphenanthridin-6(5H)-one (2c). White solid, method A: 47 mg, 59% yield; method B: 49 mg, 61% yield, mp 176-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.21-8.17 (m, 2H), 7.67 (d, J = 8.4 Hz, 1H), 7.55-7.49 (m, 2H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (J = 250 Hz), 156.0, 134.2, 132.6, 128.6, 128.2, 125.9, 124.7 (J = 7.5 Hz), 121.3 (J = 22.3 Hz), 119.6, 116.6, 114.5, 114.2 (J = 23.1 Hz), 62.9; HRMS

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(ESI): Exact mass calcd for $C_{14}H_{10}BrFNO_2$ $[M+H]^+$ 321.9873, found 321.9881.

2-Bromo-8-chloro-5-methoxyphenanthridin-6(5H)-one (2d). White solid, method A: 44 mg, 52% yield, method B: 66 mg, 78% yield, mp 224-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 1.6 Hz, 1H), 8.32 (s, 1H), 8.15 (d, J = 8.8 Hz, 1H), 7.76-7.68 (m, 2H), 7.56 (d, J = 8.8 Hz, 1H), 4.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 135.2, 134.7, 133.2, 133.0, 130.2, 128.2, 127.8, 126.0, 123.8, 119.5, 116.6, 114.6, 62.9; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}ClBrNO_2$ $[M+H]^+$ 337.9578, found 337.9573.

2,8-Dibromo-5-methoxyphenanthridin-6(5H)-one (2e). White solid, method A: 61 mg, 65% yield, mp 258-260 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (s, 1H), 8.60 (d, J = 8.8 Hz, 1H), 8.42 (s, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 4.03 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.0, 141.0, 139.8, 138.5, 135.9, 134.9, 132.8, 131.6, 131.1, 127.4, 124.5, 121.2, 120.0, 68.0; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}Br_2NO_2$ $[M+H]^+$ 381.9073, found 381.9021.

2-Bromo-9-chloro-5-methoxyphenanthridin-6(5H)-one (2f). White solid, method A: 48 mg, 57% yield; method B: 51 mg, 61% yield, mp 220-222 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, J = 8.8 Hz, 1H,), 8.27 (d, J = 1.6 Hz, 1H), 8.14 (d, J = 1.6 Hz, 1H), 7.70 (d, J = 9.2 Hz, 1H), 7.59-7.54 (m, 2H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 139.8, 135.2, 133.5, 133.1, 130.4, 129.2, 126.1, 124.9, 122.0, 119.0, 116.5, 114.6, 62.9; HRMS (ESI): Exact mass calcd for $C_{14}H_1BrClNO_2$ $[M+H]^+$ 337.9578, found 337.9598.

2-Bromo-5-methoxy-8-phenylphenanthridin-6(5H)-one (2g). White solid, method A: 81 mg, 85% yield, mp 178-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.36 (s, 1H), 8.25 (d, J = 8.8 Hz, 1H), 8.03 (dd, J = 1.6, 8.4 Hz, 1H), 7.74 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 7.6 Hz, 1H), 7.56-7.48 (m, 3H), 7.42 (t, J = 7.6 Hz, 1H), 4.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 141.5, 139.1, 134.7, 132.6, 131.5, 130.5, 129.0, 128.2, 127.2, 126.9, 126.5, 126.0, 122.7, 120.1, 116.4, 114.4, 62.9; HRMS (ESI): Exact mass calcd for $C_{20}H_{15}BrNO_2$ $[M+H]^+$ 380.0281, found 380.0282.

2-Bromo-5-methoxy-8-methylphenanthridin-6(5H)-one (2h). White solid, method A: 61 mg, 77% yield; method B: 55 mg, 69% yield, mp 176-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.28 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.62-7.57 (m, 2H), 7.51 (d, J = 8.8 Hz, 1H), 4.11 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 139.2, 134.3, 134.2, 132.1, 129.2, 128.3, 126.4, 125.7, 122.0, 120.3, 116.3, 114.3, 62.8, 21.4; HRMS (ESI): Exact mass calcd for $C_{15}H_{13}BrNO_2$ $[M+H]^+$ 318.0124, found 318.0132.

2-Bromo-5-methoxy-9-methylphenanthridin-6(5H)-one (2i). White solid, method A: 58 mg, 73% yield, mp 212-214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 8.8 Hz, 1H), 8.31 (d, J = 1.6 Hz, 1H), 7.96 (s, 1H), 7.64 (dd, J = 1.6, 8.8 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 4.11 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 143,6, 134.9, 132.5, 131.7, 130.2, 128.6, 125.9, 124.2, 122.0, 120.2, 116.2, 114.4, 62.8, 22.1; HRMS (ESI): Exact mass calcd for $C_{15}H_{13}BrNO_2$ $[M+H]^+$ 318.0124, found 318.0127.

2-Bromo-5-methoxy-[1,3]dioxolo[4,5-j]phenanthridin-6(5H)-one (2j). White solid, method A: 77 mg, 89% yield, mp 258-260 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.64 (s, 1H), 8.17 (s, 1H), 7.76 (d, J = 7.6 Hz, 1H), 7.66 (s, 1H), 7.56 (d, J = 8.4 Hz, 1H), 6.27 (s, 2H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.4, 157.7, 154.0, 138.9, 137.2, 133.6, 131.3, 126.6, 125.0, 120.8, 119.6, 110.3, 107.9, 107.3, 67.9; HRMS (ESI): Exact mass calcd for $C_{15}H_{11}BrNO_4$ $[M+H]^+$ 347.9866, found 347.9887.

2-Bromo-3-chloro-5-methoxyphenanthridin-6(5H)-one (2k). White solid, method A: 45 mg, 53% yield; method B: 48 mg, 57% yield, mp 228-230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8.0 Hz, 1H), 8.45 (s, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.80 (t, J = 7.2 Hz, 1H), 7.76 (s, 1H), 7.65 (t, J = 7.2 Hz, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 136.0, 135.6, 133.1, 131.1, 129.0, 128.8, 128.1, 126.4, 122.0, 118.6, 116.4, 114.2, 63.0; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}BrClNO_2$ $[M+H]^+$ 337.9578, found 337.9599.

2,3-Dibromo-5-methoxyphenanthridin-6(5H)-one (2l). White solid, method A: 49 mg, 51%, method B: 60 mg, 63% yield, mp 224-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 7.6 Hz, 1H), 8.45 (s, 1H), 8.17 (d, J = 7.6 Hz, 1H), 7.92 (s, 1H), 7.81 (t, J = 8.0 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 135.5, 133.1, 131.2, 129.0, 128.8, 127.8, 126.4, 126.1, 122.0, 119.2, 118.7, 117.4, 63.0; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}Br_2NO_2$ $[M+H]^+$ 381.9073, found 381.9089.

2-Bromo-5-methoxy-3-methylphenanthridin-6(5H)-one (2m). Yellow solid, method A: 42 mg, 53%, method B: 52 mg, 65% yield, mp 228-230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8.0 Hz, 1H), 8.37 (s, 1H), 8.16 (d, J = 7.6 Hz, 1H), 7.78 (t, J = 8.8 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 7.53 (s, 1H), 4.13 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 140.0, 134.9, 132.8, 131.8, 128.6, 128.3, 126.8, 126.2, 121.8, 119.2, 118.1, 114.3, 62.8, 23.5; HRMS (ESI): Exact mass calcd for $C_{15}H_{13}BrNO_2$ $[M+H]^+$ 318.0124, found 318.0130.

2-Bromo-5-methoxy-6-oxo-5,6-dihydrophenanthridin-3-yl acetate (2n). Pink solid, method A: 38 mg, 42% yield, mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 8.0 Hz, 1H), 8.44 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.79 (t, J = 7.6 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.45 (s, 1H), 4.12 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 157.0, 149.2, 136.0, 133.0, 131.3, 128.71, 128.68, 127.9, 126.2, 122.0, 117.9, 110.5, 108.1, 63.0, 20.8; HRMS (ESI): Exact mass calcd for $C_{16}H_{13}BrNO_4$ $[M+H]^+$ 362.0022, found 362.0029.

General Procedure for Chlorination.

To a solution of *N*-methoxy-[1,1'-biphenyl]- 2-carboxamide (0.25 mmol, 1 equiv) and tetrabutyl ammonium chloride (TBAC) (104 mg, 0.375 mmol, 1.5 equiv) in HFIP (1.0 mL) was added PhI (5.6 µL, 0.05 mmol, 20 mol%) and peroxyacetic acid (2.5 equiv) (32 wt.% in dilute acetic acid, 131 µL, 0.625 mmol, 2.5.0 equiv) or PIDA (201 mg, 0.625 mmol, 2.5 equiv) at 25 °C under air. The resulting mixture was stirred at 25 °C for 12 h. The reaction was monitored using TLC until the starting material was completely consumed. The reaction mixture was diluted with EtOAc (20 mL) and washed with brine (20 mL). The organic layer was dried over Na_2SO_4, and concentrated under vacuum. The resulting crude product was purified by column chromatography (hexane/EtOAc) to give the desired products **3a-f**.

2-Chloro-5-methoxyphenanthridin-6(5H)-one (3a).[19] White solid, 57 mg, 88% yield, mp 158-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 7.6 Hz, 1H), 8.17 (d, J = 7.6 Hz, 2H), 7.78 (t, J = 8.0 Hz, 1H), 7.64-7.58 (m, 2H), 7.51 (dd, J = 1.6, 8.8 Hz, 1H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 134.3, 132.8, 131.8,

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129.9, 128.9, 128.7, 128.6, 126.5, 123.0, 122.0, 119.8, 114.1, 62.8; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}ClNO_2$ $[M+H]^+$ 260.0473, found 260.0477.

2,8-Dichloro-5-methoxyphenanthridin-6(5H)-one (3b). White solid, 54 mg, 74% yield, mp 238-240 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 2.4 Hz, 1H), 8.14-8.11 (m, 2H), 7.73 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.61 (d, *J* = 9.2 Hz, 1H), 7.54 (dd, *J* = 1.6, 8.8 Hz, 1H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 135.2, 134.2, 133.2, 132.9, 130.2, 129.2, 128.2, 127.8, 123.7, 123.0, 119.1, 114.3, 62.9; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}Cl_2NO_2$ $[M+H]^+$ 294.0083, found 294.0098.

8-Bromo-2-chloro-5-methoxyphenanthridin-6(5H)-one (3c). White solid, 65 mg, 77% yield, mp 254-256 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.65-8.60 (m, 2H), 8.44 (d, *J* = 1.6 Hz, 1H), 8.07 (dd, *J* = 2.0 Hz, 8.4 Hz, 1H), 7.76-7.67 (m, 2H), 4.04 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.0, 141.0, 139.5, 136.0, 135.7, 134.9, 133.3, 132.9, 131.2, 128.8, 127.4, 124.1, 119.7, 68.0; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}BrClNO_2$ $[M+H]^+$ 337.9578, found 337.9496.

2-Chloro-5-methoxy-8-methylphenanthridin-6(5H)-one (3d). White solid, 54 mg, 79% yield, mp 152-154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.15 (d, *J* = 2.4 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.60-7.57 (m, 2H), 7.48 (dd, *J* = 2.4, 8.4 Hz, 1H), 4.12 (s, 3H), 2.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 139.2, 134.1, 134.0, 129.3, 128.8, 128.4, 126.4, 122.7, 122.0, 120.0, 114.0, 62.8, 21.4; HRMS (ESI): Exact mass calcd for $C_{15}H_{13}ClNO_2$ $[M+H]^+$ 274.0629, found 274.0634.

2-Chloro-5-methoxy-3-methylphenanthridin-6(5H)-one (3e). White solid, 48 mg, 70% yield, mp 232-234 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 8.4 Hz, 1H), 8.18 (s, 1H), 8.16 (d, *J* = 8.8 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.53 (s, 1H), 4.13 (s, 3H), 2.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 138.3, 134.3, 132.8, 131.9, 129.4, 128.6, 128.2, 126.2, 123.4, 121.8, 117.8, 114.5, 62.8, 20.7; HRMS (ESI): Exact mass calcd for $C_{15}H_{13}ClNO_2$ $[M+H]^+$ 274.0629, found 274.0634.

2,3-Dichloro-5-methoxyphenanthridin-6(5H)-one (3f). White solid, 45 mg, 61% yield, mp 164-166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 7.6 Hz, 1H), 8.23 (s, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.81 (t, *J* = 7.2 Hz, 1H), 7.76 (s, 1H), 7.65 (t, *J* = 7.2 Hz, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 135.0, 134.1, 133.1, 131.2, 129.0, 128.8, 127.2, 126.4, 124.8, 122.0, 118.3, 114.3, 63.0; HRMS (ESI): Exact mass calcd for $C_{14}H_{10}Cl_2NO_2$ $[M+H]^+$ 294.0083, found 294.0090.

General Procedure for the Synthesis of Compound 4.

To a solution of compound 2a (75.5 mg, 0.25 mmol) in DMF (2 mL) was added potassium carbonate (104 mg, 0.75 mmol), *tert*-butylammonium chloride (70 mg, 0.25 mmol), and ethyl acrylate (100 mg, 1 mmol). The reaction mixture was stirred at room temperature for 20 min, then heated at 120 °C overnight. The reaction mixture was cooled and concentrated. The resulting residue was diluted by H_2O and extracted with EtOAc (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (hexane/EtOAc) to give ethyl (*E*)-3-(5-methoxy-6-oxo-5,6-dihydrophenanthridin-2-yl) acrylate **4** as a white solid (32 mg, 40%): mp 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 7.6 Hz, 1H), 8.35 (s, 1H), 8.27 (d, *J* = 8.8 Hz, 1H), 7.82-7.74 (m, 3H), 7.68-7.61 (m, 2H), 6.52 (d, *J* = 16.4 Hz, 1H), 4.30 (q, *J* = 6.8 Hz, 2H), 4.14 (s, 3H), 1.37 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 157.1, 143.5, 137.0, 132.9, 132.4, 129.5, 128.9, 128.6, 128.5, 126.4, 123.6, 121.9, 118.7, 118.0, 113.3, 62.9, 60.6, 14.3; HRMS (ESI): Exact mass calcd for $C_{19}H_{18}NO_4$ $[M+H]^+$ 324.1230, found 324.1240.

General Procedure for the Synthesis of Compound 5.

To a solution of 2-bromo-5-methoxyphenanthridin-6(5*H*)-one (2a) (75.5 mg, 0.25 mmol) in triethylamine (2 mL) were added $Pd(PPh_3)Cl_2$ (105 mg, 0.15 mmol), CuI (47.6 mg, 0.25 mmol) and ethynyltrimethylsilane (123 mg, 1.25 mmol). The reaction mixture was stirred at 80 °C under nitrogen atmosphere for 8 h, then, saturated aqueous NH_4Cl and EtOAc were added to the reaction mixture. The organic layer was dried using $MgSO_4$, and the solvent was removed under vacuum. The crude product was purified by column chromatography to afford 5-methoxy-2-((trimethylsilyl)ethynyl)phenanthridin-6(5*H*)-one **5** (74 mg, 92%) as a white solid: mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.0 Hz, 1H), 8.35 (s, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.77 (t, *J* = 8.0 Hz, 1H), 7.66-7.58 (m, 3H), 4.12 (s, 3H), 0.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 135.6, 133.3, 132.8, 132.2, 128.5, 128.4, 127.1, 126.4, 122.1, 118.4, 118.0, 112.6, 104.3, 94.4, 62.9, 0.0; HRMS (ESI): Exact mass calcd for $C_{19}H_{20}NO_2Si$ $[M+H]^+$ 322.1258, found 322.1269.

General Procedure for the Synthesis of Compound 6.

A mixture of 2-bromo-5-methoxyphenanthridin-6(5*H*)-one (75.5 mg, 0.25 mmol), phenylboronic acid (45.8 mg, 0.375 mmol), $Pd(PPh_3)Cl_2$ (9 mg, 0.0125 mmol), K_2CO_3 (104 mg, 0.75 mmol) in dioxane/H_2O (1.5 mL/0.5 mL) was stirred at 100 °C under nitrogen atmosphere for 8 h, then cooled to room temperature. To the reaction was added H_2O (20 mL), and the resulting mixture was extracted using EtOAc (15 mL × 2), and the combined organic layers were washed using brine, and dried over Na_2SO_4. The concentrated crude product was purified by column chromatography to afford 5-methoxy-2-phenylphenanthridin-6(5*H*)-one **6** (62 mg, 86%): mp 146-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 8.0 Hz, 1H), 8.43 (s, 1H), 8.34 (d, *J* = 8.8 Hz, 1H), 7.79 (t, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 4.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 140.3, 136.4, 135.1, 132.9, 132.7, 129.0, 128.9, 128.6, 128.2, 127.5, 127.1, 126.5, 121.9, 121.7, 118.8, 113.1, 62.8; HRMS (ESI): Exact mass calcd for $C_{20}H_{16}NO_2$ $[M+H]^+$ 302.1176, found 302.1186.

General Procedure for the Synthesis of Compound 7.

To a mixture of CuCN (45 mg, 0.5 mmol), L-proline (28.8 mg, 0.25 mmol), and DMF (2 mL) under argon was added compound 2a (75.5 mg, 0.25 mmol). The mixture was stirred at 120 °C for 48 h and then cooled to room temperature. The reaction was diluted using EtOAc (15 mL) and washed by H_2O (3 × 10 mL). The organic layer was dried over Na_2SO_4, and concentrated. The crude product was purified by flash chromatography EtOAc/hexane to yield 5-methoxy-6-oxo-5,6-dihydrophenanthridine-2-carbonitrile **7** as a white solid (20 mg, 32%): mp 190-192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, *J* = 7.2 Hz, 2H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.89-7.82 (m, 2H), 7.77-7.69 (m, 2H), 4.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 138.6,

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133.4, 132.8, 131.3, 129.4, 128.8, 127.9, 126.5, 122.0, 119.0, 118.6, 113.5, 106.8, 63.1; HRMS (ESI): Exact mass calcd for $C_{15}H_{11}N_2O_2$ $[M+H]^+$ 251.0815, found 251.0821.

General Procedure for the Synthesis of Compound 8.

To a solution of compound 2a (75.5 mg, 0.25 mmol) in dioxane (1 mL) was added cesium carbonate (244 mg, 0.75 mmol), 2-(dimethylamino)acetamide (25.5 mg, 0.25 mmol), xantphos (20.3 mg, 0.035 mmol), and $Pd_2(dba)_3$ (22.9 mg, 0.025 μmol). The reaction mixture was stirred at 100 °C under nitrogen atmosphere for 36 h, then cooled to room temperature. The reaction was diluted using H_2O and extracted using EtOAc. The organic layer was dried over $MgSO_4$, and concentrated. The crude product was purified by column chromatography to afford 2-(dimethylamino)-*N*-(5-methoxy-6-oxo-5,6-dihydrophenanthridin-2-yl)acetamide **8** as a red liquid (69 mg, 85%, red liquid): ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.31 (s, 1H), 8.70 (d, J = 1.6 Hz, 1H), 8.52 (d, J = 8.0 Hz, 1H), 8.26 (d, J = 7.6 Hz, 1H), 7.75 (t, J = 7.6 Hz, 1H), 7.66 (dd, J = 2.4 Hz, 8.4 Hz, 1H), 7.61-7.56 (m, 2H), 4.11 (s, 3H), 3.14 (s, 2H), 2.42 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 156.9, 133.6, 132.6, 132.5, 132.2, 128.4, 128.2, 126.5, 122.4, 121.7, 119.0, 113.8, 113.2, 63.6, 62.7, 46.1; HRMS (ESI): Exact mass calcd for $C_{18}H_{20}N_3O_3$ $[M+H]^+$ 326.1499, found 326.1502.

General Procedure for the Synthesis of PJ34.

To a solution of compound 8 (26 mg, 0.08 mmol) in DMF (1 mL) was added NaH (60% in mineral, 10 mg, 0.24 mmol). The reaction mixture was stirred at 120 °C under nitrogen atmosphere for 1 h, and then cooled to room temperature. The reaction was diluted using H_2O and extracted using EtOAc. The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography to afford PJ34[15] as a white solid (13 mg, yield: 55%): ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.67 (s, 1H), 9.86 (s, 1H), 8.68 (s, 1H), 8.32 (t, J = 8.4 Hz, 2H), 7.89 (t, J = 7.6 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 8.8 Hz, 1H), 3.14 (s, 2H), 2.33 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.7, 165.7, 139.2, 138.8, 138.0, 137.8, 133.2, 132.8, 131.0, 127.4, 127.2, 122.6, 121.4, 118.6, 68.4, 50.6.

General Procedure for the Synthesis of other Heterocycles 10 and 12.

To a solution of *N*-([1,1'-biphenyl]-2-yl)acetamide 9 or *N*-phenylpyridin-2-amine 11 (0.25 mmol, 1 equiv) and TBAB (97 mg, 0.3 mmol, 1.2 equiv) in HFIP (1.0 mL) was added PIDA (201 mg, 0.625 mmol, 2.5 equiv) at 25 °C under air. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted using EtOAc (20 mL) and washed using brine (20 mL). The organic layer was dried over Na_2SO_4, and concentrated. The crude product was purified by column chromatography (hexane/EtOAc) to give 1-(3-bromo-9*H*-carbazol-9-yl)ethan-1-one **10** (51 mg, 71%) or 8-bromobenzo[4,5]imidazo[1,2-*a*]pyridine **12** (30.8 mg, 50%) respectively.

1-(3-Bromo-9H-carbazol-9-yl)ethan-1-one (10.)[20] mp 102-104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.8 Hz, 1H), 8.08-8.04 (m, 2H), 7.91 (d, J = 8.0 Hz, 1H), 7.55-7.48 (m, 2H), 7.39 (t, J = 8.0 Hz, 1H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 138.6, 137.4, 130.0, 128.1, 128.0, 125.2, 123.8, 122.5, 120.1, 118.0, 116.9, 115.9, 27.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}BrNO$ $[M+H]^+$ 288.0019, found 288.0019.

8-Bromobenzo[4,5]imidazo[1,2-a]pyridine (12)[21] mp 192-194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 6.8 Hz, 1H), 8.03 (s, 1H), 7.79 (d, J = 9.2 Hz, 1H), 7.67 (d, J = 9.2 Hz, 1H), 7.60 (d, J = 8.8 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 6.86 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 143.3, 129.8, 129.0, 126.4, 125.0, 121.2, 118.2, 113.8, 113.6, 110.9; HRMS (ESI): Exact mass calcd for $C_{11}H_8BrN_2$ $[M+H]^+$ 246.9865, found 246.9875.

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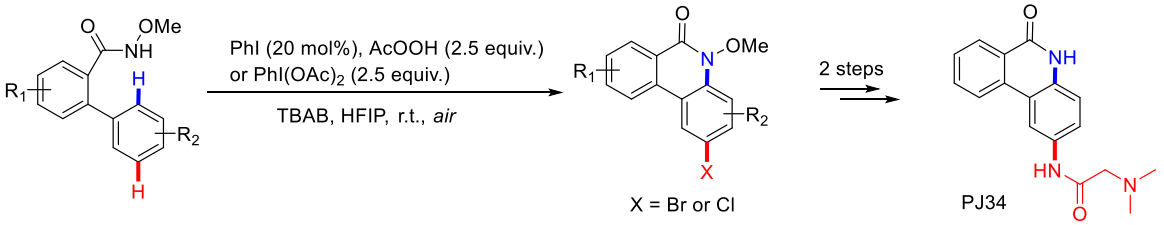

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