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Iodobenzene-Catalyzed Synthesis of Phenanthridinones via Oxidative C-H Amidation

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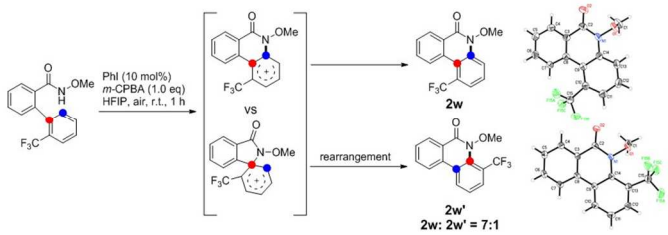
Supporting Information Placeholder



ABSTRACT: We report a novel synthesis of phenanthridinones from *N*–methoxybenzamides using an oxidative C-H amidation reaction at room temperature in open air with modest to excellent yields. This method demonstrated unprecedented substrate scope. In particular, it solved the long-standing challenge in the synthesis of phenanthridinones with sterically demanding substitutions.

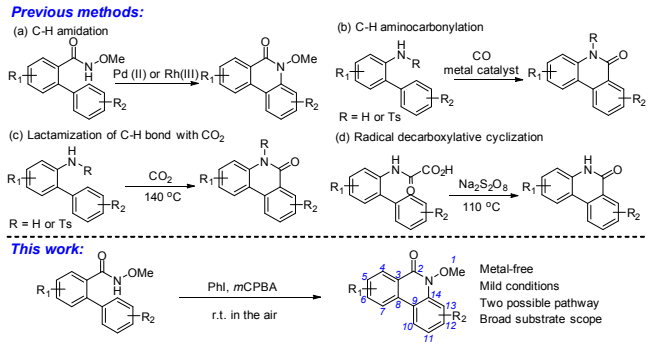
INTRODUCTION

Phenanthridinones are widely found in bioactives. Derivatives of phenanthridinone have shown anti-HIV activity by inhibiting the HIV integrase.[1] PJ34, a phenanthridinone-based inhibitor of human poly(ADP-ribose) polymerase 1, has been used as a cytoprotective[2] and neuroprotective agent.[3] The [^{11}C]PJ34 has been used as a radiotracer for imaging the role of PARP1 in necrosis.[4] 6-(5*H*)-Phenanthridinone limits the cytotoxicity of doxorubicin.[5] Crinasiadine, a natural product isolated from *Crinum asiaticum*, is known for its antimicrobial and antifungal activities.[6]

Metal-catalyzed intramolecular C-H amination has found broad applications in synthesizing heterocycles[7] such as carbazoles,[8] indoles[9] and benzimidazoles[10]. Because of its unique structure, the synthesis of phenanthridinones has attracted significant efforts.[11] Several years ago Wang,[11a] Cheng,[11b-d] and others[11e-g] reported the synthesis of phenanthridinones using Pd(II)-, Rh(III)- or Cu(I)-catalyzed C-H activation (Scheme 1a). Phenanthridinones have also been prepared by oxidative insertion of CO using metal catalyst (Scheme 1b).[11h-k] Despite their utility, metal-catalyzed processes suffer from limitations: 1) stoichiometric or excess metal reagents; 2) harsh, and usually air-sensitive conditions; and 3) narrow substrate scope. In particular, the synthesis of 7-, 10-, or 13-substituted phenanthri-dinones have not been described.

Metal-free C–H oxidative amidation have been introduced recently.[12] Yu and Xi concurrently described lactamization of aryl C-H bonds using CO_2 at 140 °C under metal-free conditions (Scheme 1c).[13] Zhang has developed radical-based transition-metal-free synthesis of phenanthridinones using decarboxylative cyclization at 110 °C in 36 h (Scheme 1d).[14] It is still highly demanding to develop practical conditions methods for efficient synthesis of phenanthridinones.

Scheme 1. Routes to Phenanthridinones via C-H Activation



Hypervalent iodine(III), as a mild oxidant for C–H activation, has been used in various transformations.[15,16] Compared to others, it demonstrated advantages such as readily availability, high stability, mild reactivity, and low toxicity.[17] Numerous iodoarene-catalyzed C–C[18] bond and C–heteroatom bond[19] formations were described. For example, in 2007 Kita reported

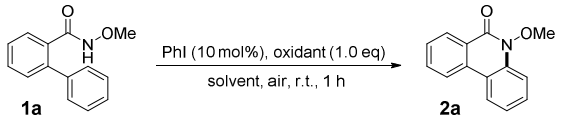
the first iodoarene-catalyzed intramolecular C–N bond formation.[20] Similar catalytic C(sp^2)−N bond formations were used to synthesize five-membered heterocyclic carbazoles,[21] pyrido[1,2-*a*]benzimidazoles[22] and indoles.[23] Recently, the first catalytic intramolecular C(sp^3)−H amidation was reported by Shi.[24] However, the C(sp^2)−H amidation using iodoarene as organocatalyst for phenanthridinones is rarely explored.[25]

In the course of our research on BCL6 inhibitors as novel anticancer agents,[26] herein we report an iodobenzene (PhI)-catalyzed synthesis of phenanthridinones using *m*CPBA as the oxidant and *N*–methoxybenzamides as the starting material. The reaction goes fast in an open vessel at room temperature, and can tolerate a wide scope of substrates with good to excellent yields. To the best of our knowledge, this is the first example of PhI-catalyzed synthesis of phenanthridinones.

RESULTS AND DISCUSSION

Treatment of **1a** with PhI (10 mol%) and *m*CPBA (1.0 equiv) in DCM at room temperature for 1 h yielded phenanthridinone (**2a**) in 64% yields (Table 1, entry 1). To optimize conditions, we first screened different solvents and found that HFIP was the best (entry 7). No measurable **2a** formation was detected without PhI (entry 8). Slightly decreased yields were observed using CH_3CO_3H as the oxidant (entry 9), while no **2a** was detected when TBHP and H_2O_2 were used (entries 10-11). In the presence of TEMPO, the reaction still showed excellent yields (entry 12), suggesting a non-radical mechanism.

Table 1. Optimization of the Reaction Conditions[a]



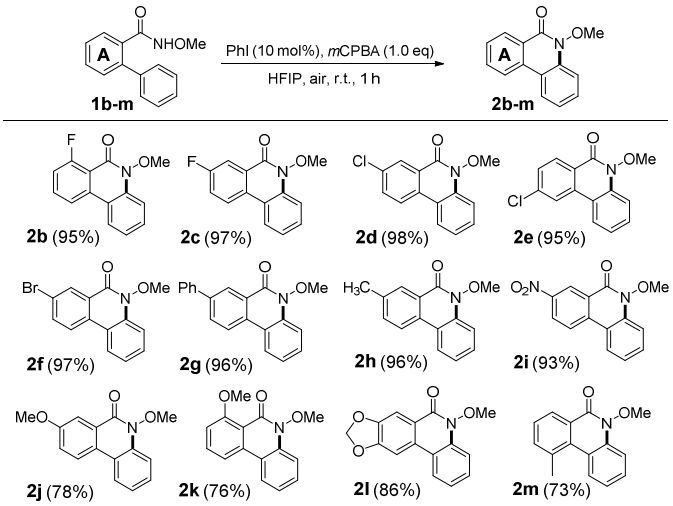
1a 2a

Entry	Catalyst	Oxidant	Solvent	Yield[b] (%)
1	PhI	*m*CPBA	DCM	64
2	PhI	*m*CPBA	CH_3CN	11
3	PhI	*m*CPBA	dioxane	5
4	PhI	*m*CPBA	TFE	89
5	PhI	*m*CPBA	MeOH	56
6	PhI	*m*CPBA	EtOH	15
7	PhI	*m*CPBA	HFIP	98
8	-	*m*CPBA	HFIP	0
9	PhI	CH_3CO_3H	HFIP	84
10	PhI	TBHP	HFIP	0
11	PhI	H_2O_2	HFIP	0
12[c]	PhI	*m*CPBA	HFIP	98

[a]A mixture of substrate **1a** (0.2 mmol), PhI (10 mol %), oxidant (1.0 equiv.) in 1.0 mL solvent was stirred at room temperature for 1 h. *m*CPBA = *meta*-chloroperoxybenzoic acid, TBHP = *tert*-butyl hydroperoxide, HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol, TFE = 2,2,2-trifluoroethanol. [b]Isolated yields. [c]TEMPO (1.0 equiv.) was included in the reaction.

We then examined the generality of the reaction (Scheme 2). Excellent yields were achieved for reactions using. Similar high yields were observed when Ph (**1g**), Me (**1h**), and NO_2 (**1i**) groups were employed. Slightly decreased yields were obtained using strong electron-donating group-containing substrates (**1j**, **1k** and **1l**), likely due to decreased electrophilicity of the corresponding *N*-methoxy-*N*-acylnitrenium intermediates (See Scheme 5, compound **4**). It is worth noting that few 7-substituted phenanthridinones are reported with available methods.[11] We were pleased to find that under our optimized conditions, 7-methyl substrate **1m** reacted to lead to the formation of **2m** in good yields.

Scheme 2. Scope of *N*-Methoxybenzamides



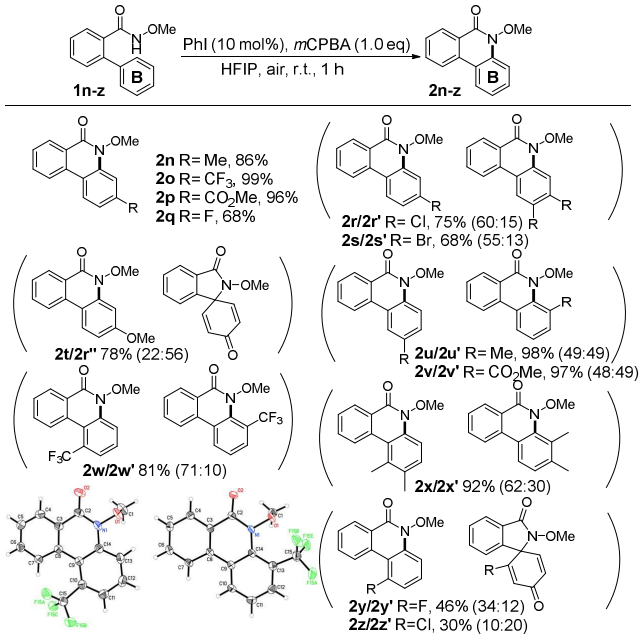
Next, we studied reactions using substrates with various B ring (Scheme 3). *p*-Me (**1n**), *p*-CF_3 (**1o**) and *p*-ester (**1p**) substrates gave excellent yields. Halogenated substrates **1q-1s** led to **2q-2s** with decreased yields. For reactions with *p*-Cl (**1r**) and *p*-Br (**1s**) substrates, in addition to **2r** and **2s**, we also isolated dihalogenated products **2r'** and **2s'** (likely through a sequential elimination - electrophilic aromatic substitution reaction),[27] along with spirocyclic ketone **2r''** (Scheme S2).[28] When *p*-OMe **1t** was used, **2t** was isolated in low yields, along with compound **2r''** as the major product.[29] The structures of **2n** and **2o**, **2q** and **2r** were confirmed by X-ray crystallography (Figures S1-S4). With the Me group moved to the *m*-position of B ring, the substrate **1u** reacted and formed two regioisomers **2u** and **2u'** with 1:1 ratio. A similar pair of regioisomers **2v** and **2v'** was obtained when the *m*-ester substituted compound **1v** was used as a substrate.

Synthesis of phenanthridinones with a 10- or 13-substituted B ring was rare.[11] We were pleased to find that the *o*-CF_3 substrate **1w,** under our conditions, generated phenanthridinone **2w** in good yields along with a small amount of the rearranged product **2w'** (Scheme 3).[30] The structures of compounds **2w** and **2w'** were confirmed by crystal X-ray crystallography. When substrate **1x** was used, the reaction also generated two regioisomers **2x** and **2x'** with a 2:1 ratio. When *o*-F substrate **1y** was used, the desired product **2y** was isolated in modest yields, along with spirocyclic side product **2y'**, which was probably formed by the addition of H_2O to the carbocation intermediate (Scheme S3). Similar result has been obtained for the *o*-Cl (**1z**) substrate. When *o*-Br substrate was used, only trace amount of the phenanthridinone was formed, along with significant amount of the spirocyclic side product (Table S1).

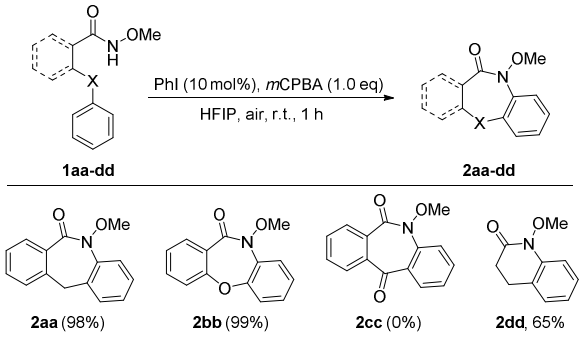
To further extend the scope of our method beyond phenanthridinones, we investigated substrates **1aa-dd**. Compounds **1aa-cc** contain an additional functional group between the two

phenyl groups (Scheme 4). When X = CH_2 (**1aa**), the reaction gave almost quantitative yield of product **2aa**.[24] Excellent yield was also shown when X = O (**2bb**). However, when ketone (**1cc**) functionalities were used, just starting material was recovered. When the A ring was removed, the resulting substrate **1dd** reacted under our conditions to yield 1-methoxy-3,4-dihydro quinolin-2(1*H*)-one (**2dd**) in good yields.

Scheme 3. Scope of *N*-Methoxybenzamides

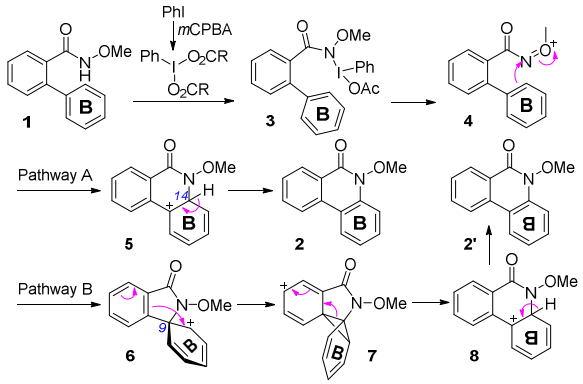


Scheme 4. Further Applications



Based on the results above, a mechanism is proposed for the formation of products **2** and **2'** (Scheme 5). Methoxybenzamide **1** reacts with hypervalent iodine(III) reagent, generated from *m*CPBA oxidation of PhI, to generate intermediate **3**, which breaks down to form the *N*-methoxy-*N*-acylnitrenium ion **4**.[31] Electrophilic attack of intermediate **4** by forming either an N1-C14 bond (pathway A) or an N1-C9 bond (pathway B) yields intermediates **5** and **6**, respectively. Elimination of intermediate **5** leads to product **2**. Rearrangement of spiro carbocation **6**, via an intermediate **7**, gives carbocation **8**, which eliminates proton to give the rearranged product **2'**.

Scheme 5. Proposed Mechanism for 2 and 2' Formation



To obtain insights into the selectivity of reaction pathways, we calculated energy differences (ΔE) between intermediates **4** and **5** and **4** and **6** for different substrates (Tables 2 and S1). For **1n** and **1o**, the direct attack (pathway A) intermediates **5** were significantly more stable than the corresponding rearrangement (pathway B) intermediates **6**, as evidenced by the large negative ΔΔE values. This result is consistent with the experimental results that only pathway A was observed for both **1n** and **1o**. Substrates **1r** indicated a small ΔΔE value, which is consistent with both pathways A and B being followed. Substrate **1t** indicated a positive ΔΔE value, indicating that pathway B is favored, consistent with the increased amount of product isolated from pathway B. Analysis of the energies of individual species shows relatively larger variation in the ΔE(**4**-**5**) values and those values show a higher correlation with the ΔΔE values (R^2 = 0.79 for ΔE(**4**-**5**) versus 0.02 for ΔE(**4**-**6**), Table S1), indicating the energetic accessibility between intermediates **4** and **5** dominates reaction flow through Pathway A versus Pathway B.

Table 2. Calculated Energy Changes

cmpd	% yield Path. A	% yield Path. B	ΔE(**4**-**5**), kcal/mol	ΔE(**4**-**6**), kcal/mol	ΔΔE,[a] kcal/mol
1n	86	0	-12.67	-3.94	-8.73
1o	99	0	-13.01	-1.72	-11.29
1r	75	15	-9.85	-4.37	-5.48
1t	22	56	4.70	-0.00	4.70

[a]ΔΔE = ΔE(**4**-**5**) - ΔE(**4**-**6**)

Given that ΔE values can explain pathway preferences we attempted to develop a predictive model that included the ΔΔE values.[32] IR frequencies, intensities and geometric parameters were also used to derive a linear regression model that can predict the free energy difference through pathways A and B. The final model utilizes IR frequency of the N-H bond (V_{NHstr}), intensities of the C=O stretching modes (I_{COstr}) and the torsion angle (Torsion) around the biphenyl bond (SI). The resulting model yields excellent predictability as shown in Figure 1. The importance of different terms was studied by evaluating the correlation when individual descriptor was removed from the model. Our results showed that the R^2 value decreased from 0.93 to 0.69, 0.69, 0.82 and 0.86 when ΔΔE, Torsion, V_{NHstr} and I_{COstr}, respectively, were dropped. Thus, ΔΔE and Torsion make the largest contributions to the reactivity.

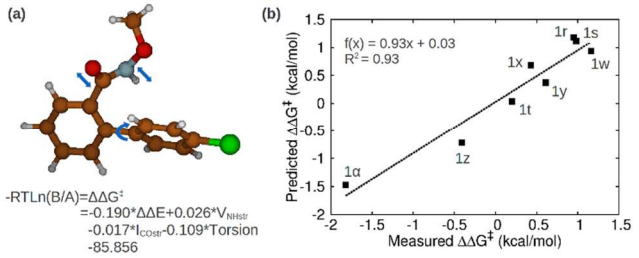


Figure 1. (a) Descriptors used to develop the regression model (formula as shown), including V_{NHstr}, I_{COstr} (double-headed arrows), and Torsion (curved arrow) as well as ΔE(**4**-**5**) and ΔE(**4**-**6**). (b) Correlation between predicted and measured ΔΔE values.

CONCLUSION

In summary we have developed a PhI-catalyzed synthesis of phenanthridinones from *N*–methoxybenzamides under mild conditions. This reaction is complementary to reported methods while demonstrating unprecedented substrate scope. The proposed mechanism was supported by computational analyses. Further application of the methodology in the preparation of BCL6 inhibitors is in progress.

EXPERIMENTAL SECTION

General Methods. 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 Procedures for Substrate Synthesis. 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 allowed to stir at 100 °C under argon atmosphere until the starting material was completely consumed (typically 20 h). The reaction mixture was then diluted with brine (25 mL). The mixture was then extracted with EtOAc (25 mL × 2), and the organic layers were combined, 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 at reflux until TLC indicated total consumption of the substrate. The solvent was removed under vacuum, and the residue was dissolved into H_2O (20 mL) and diluted with HCl (2 M) until no more precipitate was formed. The mixture was extracted with EtOAc (25 mL × 3), and the combined organic layers were dried with anhydrous 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-dimethyl aminopyridine (DMAP) (366 mg, 3 mmol) and methoxylamine hydrochloride (166 mg, 2 mmol) in one portion with stirring for 30 min. Then 1-ethyl-3-(3-dimethyl aminopropyl)carbodiimide (EDCI) (573 mg, 3 mmol) was added, and 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 with anhydrous Na_2SO_4. The solvent was removed under vacuum, and the crude product was purified by silica gel column chromatography using EtOAc/hexanes as eluent to give substrates **1**.

*N-Methoxy-[1,1'-biphenyl]-2-carboxamide (**1a**).*[11a] mp 112-114 °C; ^{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**).* mp 150-152 °C; ^{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**).* mp 112-113 °C; ^{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.

*4-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1d**).* mp 126-128 °C; ^{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.

*5-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1e**).* mp 159-160 °C; ^{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.

*4-Bromo-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1f**).* mp 145-146 °C; ^{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.

*N-Methoxy-[1,1':4',1''-terphenyl]-2'-carboxamide (**1g**).* mp 180-181 °C; ^{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**).* mp 129-130 °C; ^{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-4-nitro-[1,1'-biphenyl]-2-carboxamide (**1i**).* mp 179-181 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (br s, 1H), 8.34 (d, J = 7.6 Hz, 1H), 8.00 (s, 1H), 7.59 (d, J = 8.8 Hz, 1H), 7.49-7.44(m, 5H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.0, 147.0, 146.2, 137.4, 133.5, 131.4, 129.4, 129.2, 128.5, 125.3, 124.6, 64.2.

*N,4-Dimethoxy-[1,1'-biphenyl]-2-carboxamide (**1j**).* mp 131-132 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (br s, 1H), 7.42-7.37 (m, 5H), 7.30 (d, J = 8.4 Hz, 1H), 7.21 (s, 1H), 7.05 (dd, J = 2.4 Hz, J = 8.0 Hz, 1H), 3.86 (s, 3H), 3.53 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 159.1, 139.3, 133.1, 132.2, 131.4, 128.8, 128.7, 127.8, 117.5, 113.5, 64.0, 55.6.

*N,3-Dimethoxy-[1,1'-biphenyl]-2-carboxamide (**1k**).* mp 159-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (br s, 1H), 7.48-7.35 (m, 6H), 6.99 (d, J = 8.0 Hz, 1H), 6.93 (d, J = 7.6 Hz, 1H), 3.89 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 157.2, 142.0, 139.3, 131.0, 128.6, 128.4, 127.9, 122.1, 109.8, 64.0, 56.0.

*N-Methoxy-6-phenylbenzo[d][1,3]dioxole-5-carboxamide (**1l**).* mp 142-144 °C; ^{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.

*N-Methoxy-6-methyl-[1,1'-biphenyl]-2-carboxamide (**1m**).* mp 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (br s, 1H), 7.44-7.28 (m, 6H), 7.24 (d, J = 8.0 Hz, 2H), 3.33 (s, 3H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 139.1, 138.9, 136.7, 133.4, 132.3, 129.1, 128.8, 127.8, 127.7, 126.2, 63.7, 20.6.

*N-Methoxy-4'-methyl-[1,1'-biphenyl]-2-carboxamide (**1n**).* mp 124-125 °C; ^{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.

*N-Methoxy-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxamide (**1o**).* mp 148-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (br s, 1H), 7.67 (d, J = 7.6 Hz, 2H), 7.59-7.52 (m, 4H), 7.47-7.38 (m, 2H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 143.3, 138.8, 132.4, 130.9, 130.1, 129.8, 129.5, 129.0, 128.8, 125.4, 123.0, 63.8.

*Methyl 2'-(methoxycarbamoyl)-[1,1'-biphenyl]-4-carboxylate (**1p**).* mp 166-168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09-8.06 (m, 3H), 7.62-7.39 (m, 6H), 3.92 (s, 3H). 3.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.1, 166.7, 144.2, 139.0, 132.3, 130.9, 130.0, 129.9, 129.6, 129.0, 128.7, 128.3, 64.0, 52.3.

*4'-Fluoro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1q**).* mp 135-138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (br s, 1H), 7.61 (d, J = 6.8 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.44-7.35 (m, 4H), 7.12 (t, J = 8.4 Hz, 2H), 3.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 162.7 (J = 245.5 Hz), 138.9, 135.6, 132.3, 130.8, 130.3 (J = 9.0 Hz), 130.1, 129.0, 127.8, 115.7 (J = 20.9 Hz), 64.1.

*4'-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1r**).* mp 156-158 °C; ^{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 (**1s**).* mp 107-110 °C; ^{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,4'-Dimethoxy-[1,1'-biphenyl]-2-carboxamide (**1t**).* mp 147-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (m, 1H), 7.66 (d, J = 6.0 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.42-7.35 (m, 4H), 6.97 (d, J =8.4 Hz, 2H), 3.84 (s, 3H), 3.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 159.5, 139.5, 132.0, 131.8, 130.7, 130.1, 129.9, 129.5, 129.2, 128.5, 127.3, 127.1, 114.2, 64.0, 55.3.

*N-Methoxy-3'-methyl-[1,1'-biphenyl]-2-carboxamide (**1u**).* mp 84-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (br s, 1H), 7.65 (d, J = 7.2 Hz, 1H) 7.49 (t, J = 7.2 Hz, 1H), 7.41-7.33 (m, 2H), 7.30 (d, J = 7.2 Hz, 1H), 7.23-7.20 (m, 3H), 3.52 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 140.0, 139.5, 138.4, 132.1, 130.7, 130.0, 129.4, 129.2, 128.8, 128.7, 127.6, 125.8, 63.8, 21.4.

*Methyl 2'-(methoxycarbamoyl)-[1,1'-biphenyl]-3-carboxylate (**1v**).* mp 162-164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (br s, 1H), 8.06-8.04 (m, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.55-7.40 (m, 4H), 3.91 (s, 3H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.0, 166.7, 139.9, 139.0, 133.2, 132.3, 130.9, 130.6, 130.2, 129.6, 129.1, 128.9, 128.8, 128.1, 64.1, 52.3.

*N-Methoxy-2'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxamide (**1w**).* mp 122-123 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.00 (br s, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.59-7.45 (m, 4H), 7.36 (d, J = 7.2 Hz, 1H), 7.31 (d, J = 7.2 Hz, 1H), 3.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 138.5, 137.2, 132.6, 132.1, 131.6, 130.5, 129.9, 128.3, 128.1,127.9, 126.2, 126.1, 124.1 (q, J = 272 Hz), 63.9.

*N-Methoxy-2',3'-dimethyl-[1,1'-biphenyl]-2-carboxamide (**1x**).* mp 128-130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H), 7.73 (s, 1H), 7.58-7.37 (m, 2H), 7.30-7.13 (m, 3H), 7.12-6.98 (m, 1H), 3.42 (t, J = 1.9 Hz, 3H), 2.33 (s, 3H), 2.02 (d, J = 2.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 158.2, 139.8, 137.9, 134.7, 132.2, 130.9, 130.3, 120.0, 129.4, 127.7, 126.9, 125.9, 63.7, 20.6, 16.7.

*2'-Fluoro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1y**).* mp 106-108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (br s, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.52 (t, J = 8.0 Hz, 1H), 7.46-7.33 (m, 4H), 7.23-7.18 (m, 1H), 7.15-7.10 (m, 1H), 3.57 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 159.4 (J = 246 Hz), 134.0, 133.0, 131.3(J = 3 Hz), 131.0, 130.7, 130.0 (J = 7.5 Hz), 128.5, 128.2, 127.3(J = 16.3), 124.5, 115.6 (J = 20.8 Hz), 63.9.

*2'-Chloro-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1z**).* mp 117-119 ; °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (br s, 1H), 7.69 (d, 7.2 Hz, 1H), 7.55-7.44 (m, 3H), 7.37-7.31 (m, 4H), 3.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 138.7, 137.4, 135.2, 132.8, 132.7, 131.2, 130.7, 130.6, 129.6, 129.5, 128.5, 128.3, 127.0, 63.9.

*2'-Bromo-N-methoxy-[1,1'-biphenyl]-2-carboxamide (**1α**).* mp 110-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (br s, 1H), 7.68 (t, J = 7.6 Hz, 2H), 7.54-7.44 (m, 2H), 7.39-7.25 (m, 4H), 3.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 140.7,

139.1, 132.7, 132.5, 131.1, 130.6, 130.5, 129.7, 128.5, 128.4, 127.6, 127.0, 123.1, 63.9.

*2-Benzyl-N-methoxybenzamide (**1aa**)*.[24] mp 104-105 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (br s, 1H), 7.41-7.34 (m, 2H), 7.27-7.24 (m, 4H), 7.22-7.15 (m, 3H), 4.19 (s, 2H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 140.5, 139.8, 132.7, 131.2, 130.8, 129.0, 128.5, 127.6, 126.3, 126.2, 64.4, 38.7.

*N-Methoxy-2-phenoxybenzamide (**1bb**)*.[33] Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.12 (br s, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.44-7.37 (m, 3H), 7.24-7.19 (m, 2H), 7.08 (d, J = 8.0 Hz, 2H), 6.79 (d, J = 7.6 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8, 155.7, 155.1, 133.4, 132.4, 130.5, 125.4, 123.8, 121.7, 120.3, 117.8, 64.8.

*2-Benzoyl-N-methoxybenzamide (**1cc**)*. mp 172-174 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (br s, 1H), 7.54-7.48 (m, 4H), 7.39-7.36 (m, 3H), 7.30 (d, J = 6.8 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 145.8, 137.6, 133.4, 129.9, 128.9, 128.6, 127.9, 126.2, 123.7, 122.7, 90.8, 65.6.

*N-Methoxy-3-phenylpropanamide (**1dd**)*.[34] Colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (br s, 1H), 7.31-7.27 (m, 2H), 7.23-7.19 (m, 3H), 3.68 (s, 3H), 2.98 (t, J = 8.0 Hz, 2H), 2.56 (appt 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 140.3, 128.6, 128.4, 126.4, 64.4, 35.2, 31.3.

General Procedure for the Synthesis of Phenanthridinones. To a solution of *N*-methoxy-[1,1'-biphenyl]-2-carboxamide **1** (0.2 mmol, 1 equiv) in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (1.0 mL) was added PhI (2.3 μL, 0.02 mmol, 10 mol%) and 3-chloroperoxybenzoic acid (*m*CPBA) (tech. ca 77%, wet with H_2O, 45.0 mg, 0.2 mmol, 1.0 equiv) at 25 °C under air. The resulting mixture was stirred at 25 °C for 1 h. The reaction was monitored by 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 residue was purified by column chromatography over silica gel using petroleum ether/EtOAc as eluent to give the desired product **2**.

*5-Methoxyphenanthridin-6(5H)-one (**2a**)*.[11a,11c,1d] White solid, 44 mg, 98% yield, mp 128-129 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, J = 7.6 Hz, 1H), 8.20 (dd, J = 2.0 Hz, J = 8.0 Hz, 2H), 7.71 (t, J = 8.0 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.54-7.50 (m, 2H), 7.30-7.26 (m, 1H), 4.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 136.0, 133.1, 132.8, 130.1, 128.7, 128.3, 126.5, 123.4, 122.1, 118.7, 112.8, 62.9.

*7-Fluoro-5-methoxyphenanthridin-6(5H)-one (**2b**)*. White solid, 46 mg, 95% yield, mp 148-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (d, J = 8.0 Hz, 1H), 8.06 (d, J = 8.8 Hz, 1H), 7.73-7.57 (m, 3H), 7.33 (t, J = 7.6 Hz, 1H), 7.24 (t, J = 8.8 Hz, 1H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.0 (J = 263 Hz), 154.6, 136.1, 135.7, 133.5 (J = 10.4 Hz), 130.7, 123.5 (J = 47.6 Hz), 117.8 (J = 4.5 Hz), 117.4, 115.6, 115.4, 115.1, 112.5, 62.7; IR (KBr): 3054, 2925, 1742, 1685, 1594, 1460, 1377, 1293, 1278, 1192, 1177, 1124, 1028, 916, 811, 690, 673, 589, 548; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}FNO_2$ $[M+H]^+$ 244.0768, found 244.0764.

*8-Fluoro-5-methoxyphenanthridin-6(5H)-one (**2c**)*. White solid, 47 mg, 97% yield, mp 142-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23-8.19 (m, 1H), 8.15-8.12 (m, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.46-7.41 (m, 1H), 7.31 (t, J = 8.0 Hz, 1H), 4.08 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.4, 160.9, 156.4, 135.3, 129.8, 129.5, 128.2, 124.52, 124.50, 123.5, 123.1, 121.1, 120.9, 117.9, 114.1, 113.9, 112.7, 62.8; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}FNO_2$ $[M+H]^+$ 244.0768, found 244.0778.

*8-Chloro-5-methoxyphenanthridin-6(5H)-one (**2d**)*.[35] White solid, 51 mg, 98% yield, mp 180-182 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, J = 2.4 Hz, 1H), 8.22 (d, J = 8.4 Hz, 2H), 7.75-7.69 (m, 2H), 7.62 (t, J = 8.0 Hz 1H), 7.38 (t, J = 8.4 Hz, 1H), 4.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 135.6, 134.3, 133.0, 131.4, 130.3, 128.0, 127.5, 123.7, 123.5, 123.2, 117.8, 112.8, 62.8.

*9-Chloro-5-methoxyphenanthridin-6(5H)-one (**2e**)*.[11a,11c] White solid, 49 mg, 95% yield, mp 179-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, J = 8.4 Hz, 1H), 8.21 (s, 1H), 8.17 (d, J = 7.6 Hz, 1H), 7.68-7.59 (m, 2H), 7.54-7.52 (m, 1H), 7.35 (t, J = 7.2 Hz, 1H), 4.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 139.4, 136.2, 134.4, 130.7, 130.3, 128.5, 124.7, 123.4, 123.3, 121.9, 117.4, 112.8, 62.8.

*8-Bromo-5-methoxyphenanthridin-6(5H)-one (**2f**)*.[11c,11d] White solid, 59 mg, 97% yield, mp 184-185 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, J = 1.6 Hz, 1H), 8.22 (d, J = 7.6 Hz 1H), 8.14 (d, J = 9.6 Hz, 1H), 7.87 (dd, J = 2.4 Hz, J = 9.6 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.37 (t, J = 8.0 Hz, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 135.7, 131.8, 131.2, 130.4, 127.7, 123.8, 123.5, 123.2, 122.2, 117.9, 112.8, 62.8.

*5-Methoxy-8-phenylphenanthridin-6(5H)-one (**2g**)*. White solid, 57.6 mg, 96% yield, mp 155-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, J = 2.4 Hz, 1H), 8.33 (d, J = 8.8 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.02 (dd, J = 1.6 Hz, J = 8.4 Hz, 1H), 7.76-7.68 (m, 3H), 7.59 (t, J = 8.0 Hz, 1H), 7.50 (t, J = 7.6 Hz, 2H), 7.43-7.35 (m, 2H), 4.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.3, 140.8, 139.4, 135.7, 131.8, 131.3, 129.9, 129.0, 128.0, 127.2, 126.7, 126.4, 123.3, 123.2, 122.6, 118.4, 112.6, 62.7; HRMS (ESI): Exact mass calcd for $C_{20}H_{16}NO_2$ $[M+H]^+$ 302.1176, found 302.1172.

*5-Methoxy-8-methylphenanthridin-6(5H)-one (**2h**)*.[11a,11c,11d] White solid, 46 mg, 96% yield, mp 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 1H), 8.21 (d, J = 7.6 Hz, 1H), 8.05 (d, J = 8.8 HZ, 1H), 7.57 (d, J = 8.4 Hz, 1H), 7.49-7.44 (m, 2H), 7.24 (t, J = 8.0 Hz, 1H), 4.05 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.3, 138.3, 135.4, 133.9, 130.4, 129.4, 128.2, 126.1, 123.1, 122.9, 121.9, 118.6, 112.5, 62.6, 21.3.

*5-Methoxy-8-nitrophenanthridin-6(5H)-one (**2i**)*.[11c-d] Yellow solide, 50 mg, 93% yield, mp 267-269 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (d, J = 2.0 Hz, 1H), 8.57 (dd, J = 2.4 Hz, J = 9.2 Hz, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.30 (d, J = 8.0 Hz, 2H), 7.74-7.71 (m, 2H), 7.46-7.42 (m, 1H), 4.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.9, 146.9, 137.9, 136.9, 132.2, 127.0, 126.6, 124.6, 124.4, 123.9, 123.6, 116.9, 113.1, 63.0.

*5,8-Dimethoxyphenanthridin-6(5H)-one (**2j**)*.[36] Yellowish-brown solid, 40 mg, 78% yield, mp 138-140 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20-8.16 (m, 2H), 7.95 (d, J = 2.4 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 8.0 Hz, 1H), 7.37-7.32 (m, 2H), 4.14 (s, 3H), 3.97 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.5, 157.1, 134.7, 128.8, 127.6, 126.4, 123.7, 123.2, 122.6, 122.5, 118.6, 112.5, 108.8, 62.7, 55.8.

*5,7-Dimethoxyphenanthridin-6(5H)-one (**2k**)*.[36] White solid, 39 mg, 76% yield, mp 164-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J = 7.6 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 7.61-7.56 (m, 2H), 7.29 (d, J = 7.6 Hz, 1H), 7.05

(d, J = 8.8 Hz, 1H), 4.11 (s, 3H), 4.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 156.1, 136.3, 135.9, 133.2, 130.2, 123.8, 122.7, 117.8, 115.4, 114.1, 123.8, 112.2, 110.3, 62.5, 56.5.

5-Methoxy-[1,3]dioxolo[4,5-J]phenanthridin-6(5H)-one ***(2l)***.[36] White solid, 46.5 mg, 86% yield, mp 235-237 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0 Hz, 1H), 7.89 (s, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.54 (t, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 6.13 (s, 2H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 152.4, 148.5, 135.0, 129.8, 129.2, 123.0, 122.8, 121.8, 118.3, 112.5, 106.5, 102.1, 100.7, 62.7.

5-Methoxy-10-methylphenanthridin-6(5H)-one ***(2m)***. White solid, 35 mg, 73% yield, mp 120-122 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, J = 7.6 Hz, 1H), 8.47 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.63-7.56 (m, 2H), 7.49 (t, J = 8.0 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 4.13 (s, 3H), 2.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 137.1, 135.9, 134.9, 132.4, 129.1, 127.8, 127.3, 127.0, 122.4, 120.0, 112.4, 62.6, 26.2; HRMS (ESI): Exact mass calcd for $C_{15}H_{14}NO_2$ $[M+H]^+$ 240.1019, found 240.1025.

5-Methoxy-3-methylphenanthridin-6(5H)-one ***(2n)***.[11a, 11c,11d] White solid, 41 mg, 86% yield, mp 146-148 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, J = 7.6 Hz, 1H), 8.22 (d, J = 7.6 Hz, 1H), 8.13 (d, J = 7.6 Hz, 1H), 7.75 (t, J = 8.0 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.16 (d, J = 8.4 Hz, 1H), 4.14 (s, 3H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.7, 135.8, 131.0, 128.3, 127.8, 123.7, 122.8, 121.1, 119.6, 118.3, 116.9, 111.4, 107.9, 57.9, 17.1.

5-Methoxy-3-(trifluoromethyl)phenanthridin-6(5H)-one ***(2o)***. White solid, 58 mg, 99% yield, mp 184-187 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 8.0 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 7.93 (s, 1H), 7.85 (t, J = 8.0 Hz, 1H), 7.69 (t, J = 8.0 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 4.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 157.1, 135.9, 133.0, 131.9, 131.8, 131.6, 129.3, 128.7, 126.9, 125.1, 124.0, 122.4, 121.2, 119.6, 109.94, 109.89, 63.0. HRMS (ESI): Exact mass calcd for $C_{15}H_{11}F_3NO_2$ [M+H]+ 294.0736, found 294.0740.

Methyl 5-methoxy-6-oxo-5,6-dihydrophenanthridine-3-carboxylate ***(2p)***.[11a] White solid, 54 mg, 96% yield, mp 195-196 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (d, J = 7.6 Hz, 1H),8.34-8.30 (m, 3H), 7.99 (d, J = 8.0 Hz, 1H), 7.82 (t, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 4.18 (s, 3H), 4.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 157.1, 135.7, 132.9, 132.0, 131.2, 129.2, 128.7, 127.0, 123.9, 122.6, 122.2, 114.0, 63.0, 52.6.

3-Fluoro-5-methoxyphenanthridin-6(5H)-one ***(2q)***.[11d] White solid, 33 mg, 68% yield, mp 148-150 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, J = 8.0 Hz, 1H), 8.24-8.17 (m, 2H), 7.78 (t, J = 7.2 Hz, 1H), 7.59 (t, J = 8.0 Hz, 1H), 7.38-7.26 (m, 1H), 7.08-7.04 (m, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.8 (J = 247 Hz), 157.4, 137.3 (J = 10.5 Hz), 132.9, 132.5, 128.6, 127.9, 125.6, 125.3 (J = 10.4 Hz), 121.7, 114.9, 110.8 (J = 23.8 Hz), 99.8 (J = 26.8 Hz), 62.8.

3-Chloro-5-methoxyphenanthridin-6(5H)-one ***(2r)***.[11a] *and 2,3-dichloro-5-methoxy phenanthridin-6(5H)-one* ***(2r')***. *(4:1)* White solid, 39 mg, 75% yield, ^{1}H NMR (400 MHz, $CDCl_3$): 8.52 (d, J = 8.0 Hz, 1H), 8.19-8.12 (m, 2H), 7.78 (t, J = 7.6 Hz, 1H), 7.65-7.58 (m, 2H), 7.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): 157.2, 156.9, 136.6, 136.0, 135.0, 134.0, 133.1, 132.9, 132.2, 131.2, 129.0, 128.7, 128.6, 128.3, 127.2, 126.4, 126.0, 124.8, 124.5, 123.5, 122.0, 121.9, 118.3, 117.0, 114.3, 112.6, 63.0, 62.9. HRMS (ESI): Exact mass calcd for $C_{14}H_{11}ClNO_2$ $[M+H]^+$ 260.0473, found 260.0468; Exact mass calcd for $C_{14}H_{10}Cl_2NO_2$ $[M+H]^+$ 294.0083, found 294.0090.

2,3-Dibromo-5-methoxyphenanthridin-6(5H)-one ***(2s)***.[11a,11c] *and 2,3-dibromo-5-methoxyphenanthridin-6(5H)-one* ***(2s')***. (4:1) White solid, 41mg 68% yield, ^{1}H NMR (400 MHz, $CDCl_3$): 8.53 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.90-7.76(m, 2H), 7.62(t, J = 7.2 Hz, 1H), 7.44 (dd, J = 1.6 Hz, J = 8.4 Hz, 1H), 4.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 157.1, 136.6, 133.1, 132.9, 132.3, 129.0, 128.7, 128.6, 128.4, 127.8, 126.3, 126.1, 124.6, 124.0, 122.0, 121.9, 117.4, 115.5, 63.0, 62.9; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}BrNO_2$ $[M+H]^+$ 303.9968, found 303.9976; Exact mass calcd for $C_{14}H_{10}Br_2NO_2$ $[M+H]^+$ 381.9073, found 381.9074.

3,5-Dimethoxyphenanthridin-6(5H)-one ***(2t)***.[11a] White solid, 11 mg, 22% yield, mp 145-148 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 7.6 Hz, 1H), 7.74 (t, J = 8.8 Hz, 1H), 7.53 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 2.0 Hz, 1H), 6.93 (dd, J = 8.4 Hz, J = 2.4 Hz, 1H), 4.14 (s, 3H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3, 157.7, 137.2, 133.2, 132.7, 128.5, 126.9, 125.0, 124.7, 121.3, 111.9, 110.7, 96.7, 62.6, 55.7.

2'-Methoxyspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione ***(2r'')***. Yellowish-brown solid, 27 mg, 56% yield, mp 198-200 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.6 Hz, 1H), 7.63-7.54 (m, 2H), 7.19 (d, J = 7.6 Hz, 1H), 6.64 (d, J = 10.0 Hz, 2H), 6.51 (d, J = 10.0 Hz, 2H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.6, 165.4, 145.6, 139.3, 133.5, 131.6, 130.2, 129.3, 125.0, 122.8, 66.1, 65.1; HRMS (ESI): Exact mass calcd for $C_{14}H_{12}NO_3$ $[M+H]^+$ 242.0812, found 242.0824.

5-Methoxy-2-methylphenanthridin-6(5H)-one ***(2u)***. *and 5-methoxy-4-methyl phenanthridin-6(5H)-one* ***(2u')***.[35] Yellowish-brown solid, 47 mg, 98% yield, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (t, J = 8.0 Hz, 2H), 8.26 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 8.0 Hz, 1H), 8.05 (s, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.61-7.55 (m, 3H), 7.41-7.35 (m, 2H), 7.23 (t, J = 8.0 Hz, 1H), 4.12 (s, 3H), 3.97 (s, 3H), 2.79 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.5, 157.1, 134.9, 134.6, 133.6, 133.4, 132.9, 132.8, 132.7, 132.5, 131.0, 128.5, 128.3, 128.0, 127.9, 126.3, 125.9, 124.4, 123.3, 122.3, 121.9, 119.9, 118.5, 112.6, 63.0, 62.6, 23.4, 21.1; HRMS (ESI): Exact mass calcd for $C_{15}H_{14}NO_2$ $[M+H]^+$ 240.1019, found 240.1027.

Methyl 5-methoxy-6-oxo-5,6-dihydrophenanthridine-2-carboxylate ***(2v)***. *and methyl 5-methoxy-6-oxo-5,6-dihydrophenanthridine-4-carboxylate* ***(2v')***. White solid, 55 mg, 97% yield, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.99 (s, 1H), 8.50-8.47 (m, 2H), 8.32 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.17 (dd, J = 1.6 Hz, J = 8.4 Hz 1H), 7.79-7.73 (m, 2H), 7.65 (d, J = 8.8 Hz, 1H), 7.61-7.56 (m, 2H), 7.46 (d, J = 6.4 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 4.16 (s, 3H), 4.00 (s, 3H), 3.98 (s, 3H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 166.4, 157.4, 138.8, 133.0, 132.9, 132.6, 132.5, 130.8, 128.9, 128.5, 128.4, 126.2, 126.1, 125.4, 124.9, 124.5, 122.9, 122.2, 122.1, 120.7, 119.4, 118.2, 112.6, 63.9, 63.0, 52.7, 52.4. HRMS (ESI): Exact mass calcd for $C_{16}H_{14}NO_4$ [M+H]+ 284.0917, found 284.0920.

5-Methoxy-1-(trifluoromethyl)phenanthridin-6(5H)-one ***(2w)***. White solid, 41.6 mg, 71% yield, mp 126-128 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 2H), 7.77-7.74 (m, 3H), 7.56-7.51 (m, 4H), 7.50-7.43 (m,

2H), 7.31 (t, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.5, 140.2, 138.7, 133.0, 132.0, 129.6, 128.9, 128.4, 127.8, 127.4, 124.0, 123.3, 122.1, 121.8, 110.5. HRMS (ESI): Exact mass calcd for $C_{15}H_{11}F_3NO_2$ $[M+H]^+$ 294.0736, found 294.0740.

5-Methoxy-4-(trifluoromethyl)phenanthridin-6(5H)-one ***(2w')***. White solid, 6 mg, 10% yield, mp 155-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.57 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 8.8 Hz, 1H), 8.30 (d, J = 7.6 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.84 (t, J = 8.0 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.43 (t, J = 8.0 Hz, 1H), 3.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 134.2, 133.2, 132.4, 130.1, 130.0, 129.93, 129.85, 128.9, 128.5, 127.2, 126.1, 125.2, 122.5, 122.3, 120.7, 62.9; HRMS (ESI): Exact mass calcd for $C_{15}H_{11}F_3NO_2$ $[M+H]^+$ 294.0736, found 294.0740.

5-Methoxy-1,2-dimethylphenanthridin-6(5H)-one ***(2x)****. and 5-methoxy-3,4-dimethylphenanthridin-6(5H)-one* ***(2x')***. (2:1) White solid, 46.5 mg, 92% yield, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 3.86 (s, 3H), 2.64 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.9, 157.0, 140.5, 135.1, 134.8, 134.6, 134.0, 133.4, 133.1, 132.9, 132.6, 131.2, 131.0, 128.4, 127.5, 127.4, 127.3, 127.1, 126.0, 125.7, 123.4, 121.9, 120.4, 118.8, 118.5, 109.8, 62.5, 62.3, 29.7, 21.8, 21.1, 17.6; HRMS (ESI): Exact mass calcd for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1176, found 254.1191.

1-Fluoro-5-methoxyphenanthridin-6(5H)-one ***(2y)***. White solid, 17 mg, 34% yield, mp 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (dd, J = 2.4 Hz, J = 8.4 Hz, 1H), 8.60 (d, J = 8.0 Hz, 1H), 7.79 (t, J = 8.0 Hz, 1H), 7.63 (t, J = 7.6 Hz, 1H), 7.52-7.50 (m, 2H), 7.10-7.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1 (J = 251 Hz), 157.0, 137.3 (J = 7.5 Hz), 133.1, 130.7, 129.9 (J = 11.9 Hz), 128.3 (J = 13.4 Hz), 127.0, 126.8, 126.2, 110.7 (J = 23.8 Hz), 108.4, 108.2 (J = 20.9 Hz), 62.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}FNO_2$ $[M+H]^+$ 244.0768, found 244.0763.

2-Fluoro-2'-methoxyspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione ***(2y')***. White solid, 6 mg, 12% yield, mp 153-156 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 6.8 Hz, 1H), 7.65-7.61 (m, 2H), 7.25 (d, J = 9.2 Hz, 1H), 6.59-6.50 (m, 2H), 6.25 (d, J = 12.4 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 186.3 (J = 14.9 Hz), 171.6, 167.4 (J = 272.3 Hz), 141.8, 137.5, 133.7, 131.0, 130.8, 129.7, 125.1, 122.3, 112.6 (J = 8.9 Hz), 65.8, 65.3; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}FNO_3$ $[M+H]^+$ 260.0717, found 260.0716.

1-Chloro-5-methoxyphenanthridin-6(5H)-one ***(2z)***. White solid, 5 mg, 10% yield, mp 156-157 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.49 (d, J = 8.8 Hz, 1H), 8.64 (d, J = 7.6 Hz, 1H), 7.80 (td, J = 1.6 Hz, J = 8.0 Hz, 1H), 7.71-7.64 (m, 2H), 7.49-7.42 (m, 2H), 4.12 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 137.9, 132.0 (2C), 129.2, 128.5, 128.4, 127.3, 126.9, 126.7, 116.3, 111.6 (2C), 62.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}ClNO_2$ $[M+H]^+$ 260.0473, found 260.0479.

2-Chloro-2'-methoxyspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione ***(2z')***. White solid, 11 mg, 20% yield, mp 173-175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 7.2 Hz, 1H), 7.63-7.59 (m, 2H), 7.18 (d, J = 8.0 Hz, 1H), 6.73-6.69 (m, 2H), 6.54 (d, J = 9.6 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.4, 166.0, 152.1, 144.9, 138.9, 133.8, 131.8, 130.7, 129.8, 124.9, 122.1, 68.0, 65.6; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}ClNO_3$ $[M+H]^+$ 276.0422, found 276.0431.

2-Bromo-2'-methoxyspiro[cyclohexane-1,1'-isoindoline]-2,5-diene-3',4-dione ***(2a)***. White solid, 14 mg, 22% yield, mp 156-158 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, J = 7.2 Hz, 1H), 7.65-7.58 (m, 2H), 7.16 (d, J = 6.8 Hz, 1H), 6.98 (s, 1H), 6.77 (d, J = 10.0 Hz, 1H), 6.55 (d, J = 10.0 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.6, 165.9, 145.3, 145.2, 139.4, 136.0, 133.8, 130.6, 130.5, 129.8, 124.9, 122.2, 68.7, 65.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{11}BrNO_3$ $[M+H]^+$ 319.9917, found 319.9917.

5-Methoxy-5,11-dihydro-6H-dibenzo[b,e]azepin-6-one ***(2aa)***.[24] White solid, 47 mg, 98% yield, mp 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, J = 7.6 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.30-7.21 (m, 4H), 7.16 (t, J = 8.0 Hz, 1H), 4.13 (br, 1H), 3.91 (s, 3H), 3.67 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 141.5, 137.9, 134.8, 132.2, 131.1, 130.9, 127.5, 127.3, 127.0, 126.7, 126.6, 120.6, 62.7, 39.0.

10-Methoxydibenzo[b,f][1,4]oxazepin-11(10H)-one ***(2bb)***.[33] Colorless oil, 48 mg, 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.6 Hz, 1H), 7.55-7.47 (m, 2H), 7.28-7.18 (m, 5H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.6, 159.7, 151.4, 134.2, 132.6, 132.1, 127.0, 126.0, 125.4, 124.4, 121.2, 120.5, 120.4, 62.7; HRMS (ESI): Exact mass calcd for $C_{14}H_{12}NO_3$ $[M+H]^+$ 242.0812, found 242.0815.

1-Methoxy-3,4-dihydroquinolin-2(1H)-one ***(2dd)***.[34] Colorless oil, 29 mg, 65% yield, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.16 (d, J = 6.8 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 3.91 (s, 3H), 2.91 (t, J = 8.0 Hz, 2H), 2.70 (t, J = 8.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 137.8, 127.7, 124.3, 123.5, 112.2, 62.5, 31.5, 24.8.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge via the Internet at http://pubs.acs.org. Mechanistic study results, X-ray crystallographic data, computational calculation details, copies of NMR spectra

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Notes

The authors declare no competing financial interest.

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