JOC The Journal of Organic Chemistry

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Mechanochemical-Cascaded C−N Cross-Coupling and Halogenation Using *N*-Bromo- and *N*-Chlorosuccinimide as Bifunctional Reagents

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Cite This: https://doi.org/10.1021/acs.joc.1c01742 Read Online

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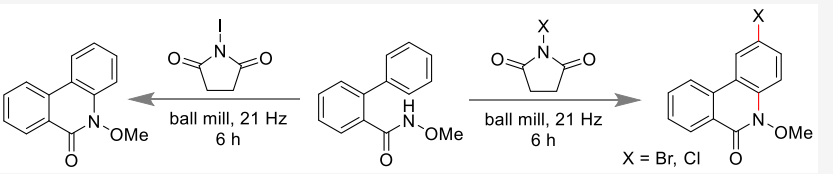


ABSTRACT: Exploration of alternative energy sources for chemical transformations has gained significant interest from chemists, and mechanochemistry is one of those sources. Herein, we report the use of *N*-bromosuccinimides (NBS) and *N*-chlorosuccinimides (NCS) as bifunctional reagents for a cascaded C−N bond formation and subsequent halogenation reactions. Under the solvent-free mechanochemical (ball-milling) conditions, the synthesis of a wide range of phenanthridinone derivatives from *N*-methoxy-[1,1′-biphenyl]-2-carboxamides is accomplished. During the reactions, NBS and NCS first assisted the oxidative C−N coupling reaction and subsequently promoted a halogenation reaction. Thus, the role of NBS and NCS was established to be bifunctional. Overall, a mild, solvent-free, convenient, one-pot, and direct synthesis of various bromo- and chloro-substituted phenanthridinone derivatives was achieved.

INTRODUCTION

The utilization of readily accessible chemicals for the convenient and economical synthesis of functional materials and bioactive molecules is the state-of-the-art practice in synthetic organic chemistry. Recently, nontraditional energy sources such as microwave,[1,2] visible light,[3] electrochemical,[4] mechanochemical,[5,6] and ultrasonication[7,8] have become popular. The mechanochemical approach also offers a robust and sustainable strategy in organic synthesis.[9−11] The primary advantage of mechanochemical synthesis is the solvent-free condition,[12] which can avoid issues like high reaction temperature and solubility.[13] Toward that end, quantitative conversion, minimum purification process, and less undesired side products carry extra significance to this practice.[14] In addition, the mechanochemical reactions are expected to follow the "Twelve Principles of Green Chemistry".[15] IUPAC recognizes that mechanochemistry is one of 10 innovative technologies.[16] The mechanochemical approaches are widely used in research areas such as the synthesis of heterocyclic compounds,[17,18] synthesis of metal complexes,[19] molecular syntheses,[10,20] supramolecular chemistry,[21,22] asymmetric organic synthesis,[23−25] etc. In addition, solid-state transformations such as C−H borylation,[26] C−H bond amidation,[27] and C−C[28,29] and C−N[30] bond formations have been well explored in mechanochemistry.[30]

Recently, bifunctional reagents[31] have gained popularity because multistep reactions can be done in minimum steps and cost-effective ways.[32−34] The bifunctional systems are well-known in supramolecular chemistry,[35−37] material science,[38] organic synthesis,[34] catalysis,[39] anion-relay chemistry,[40] etc. Wu and co-workers reported an oxidative aminohalogenation of maleimides using haloamines as bifunctional reagent.[41] In addition, tandem electrochemical cyclization, trifluoromethylation, and SO_2 insertion of *N*-cyanamide alkenes were achieved using CF_3SO_2Na as a bifunctional reagent in which CF_3SO_2Na acted as both CF_3 and SO_2 sources.[42] However, the use of *N*-bromosuccinimide (NBS) and *N*-chlorosuccinimide (NCS) as bifunctional reagents in organic synthesis is relatively unknown, if any. Recently, we reported the utilization of *N*-iodosuccinimide (NIS) as a bifunctional reagent in (*E*)-selective sulfonylation reaction of styrenes.[43] We have shown herein the use of NBS and NCS as bifunctional reagents for one-pot synthesis of phenanthridinones via a cascaded intramolecular oxidative C−N coupling and subsequent halogenation reaction under solvent-free ball-milling mechanochemical conditions.

Phenanthridinones are important *N*-containing heterocycles omnipresent in many natural products and pharmacologically active compounds (Figure 1a). The molecules *N*-methylcrinasiadine and phenaglydon[44] are potent HIV-1 integrase inhibitors.[45] Oxynitidine derivatives have shown TOP1 and TDP1 inhibitor activity.[46] Amaryllidaceae alkaloids[47] like

Special Issue: Enabling Techniques for Organic Synthesis

Received: July 22, 2021

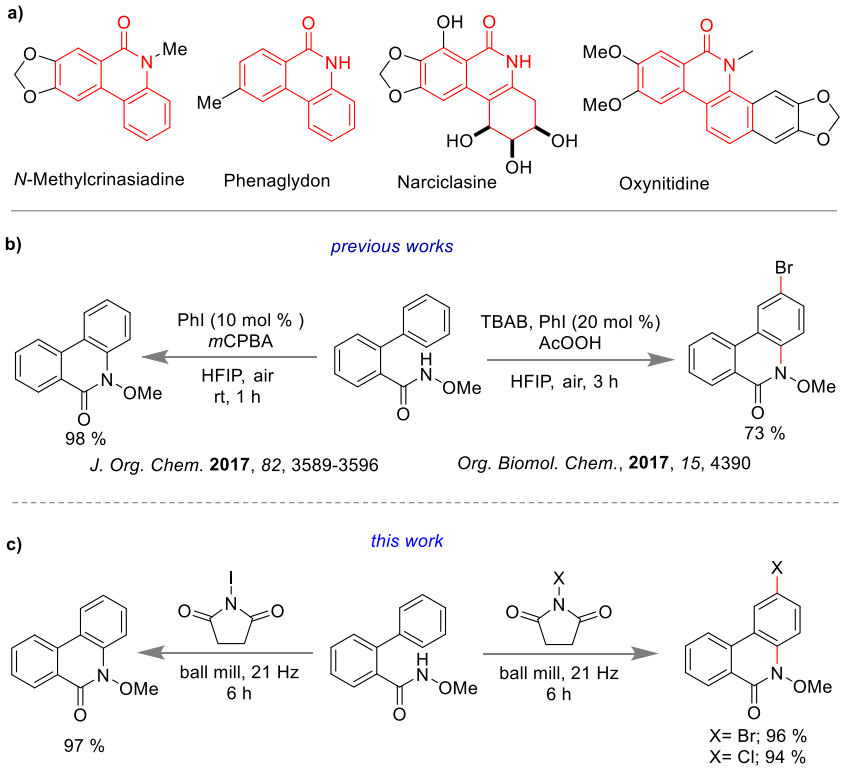
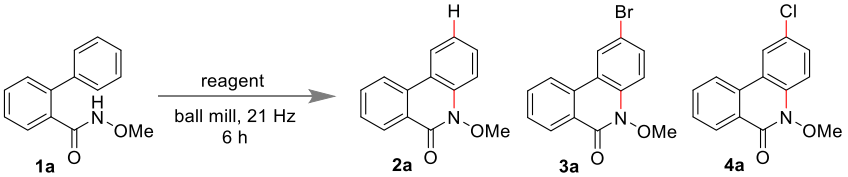


Figure 1. (a) Phenanthridinones containing biologically active drug molecules. (b) Sequential one-pot synthesis of bromophenanthridinones using tetrabutylammonium bromide and PhI-peracetic acid (right-hand side) and the use of PhI-*m*CPBA combination for oxidative C−N coupling (left-hand side).[58] (c) Our work is based on the mechanochemical synthesis of phenanthridinones or their halogenated derivatives using *N*-halosuccinimides.

Table 1. Optimization of Reaction Conditions[a]



entry	reagent (equiv)	product (yield, %)
1	NBS (1.0)	**2a**:**3a** (1:3)
2	NBS (1.5)	**2a**:**3a** (1:10)
3	NBS (2)	**3a** (96)
4	NCS (1)	**2a**:**4a** (1:3)
5	NCS (2)	**4a** (94)
6	NIS (1)	**2a** (69)
7	NIS (1.5)	**2a** (84)
8	NIS (2)	**2a** (97)
9	PIDA (2)	**2a** (60)
10	PIFA (2)	**2a** (54)
11	TBAI, $K_2S_2O_8$ (2)	**2a** (0)
12	TBAI, $(NH_4)_2S_2O_8$ (2)	**2a** (0)
13	I_2 (2)	**2a** (0)
14	DDQ (2)	**2a** (35)
15	Oxone (2)	**2a** (52)
16[b]	NIS (2)	**2a** (91)
17[c]	NIS (2)	**2a** (97)

[a]All reactions are carried out on an 0.18 mmol scale of **1a** for 6 h. [b]Reaction was carried out at 16 Hz for 6 h. [c]Reaction was carried out at 25 Hz for 6 h.

narciclasine[48] exhibit antimitotic activity and antitumor effects[49] and inhibit angiogenic processes.[50]

In the synthesis of phenanthridinones, the notable examples are palladium-catalyzed oxidative annulation of *N*-methoxyben-

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J. Org. Chem. XXXX, XXX, XXX−XXX

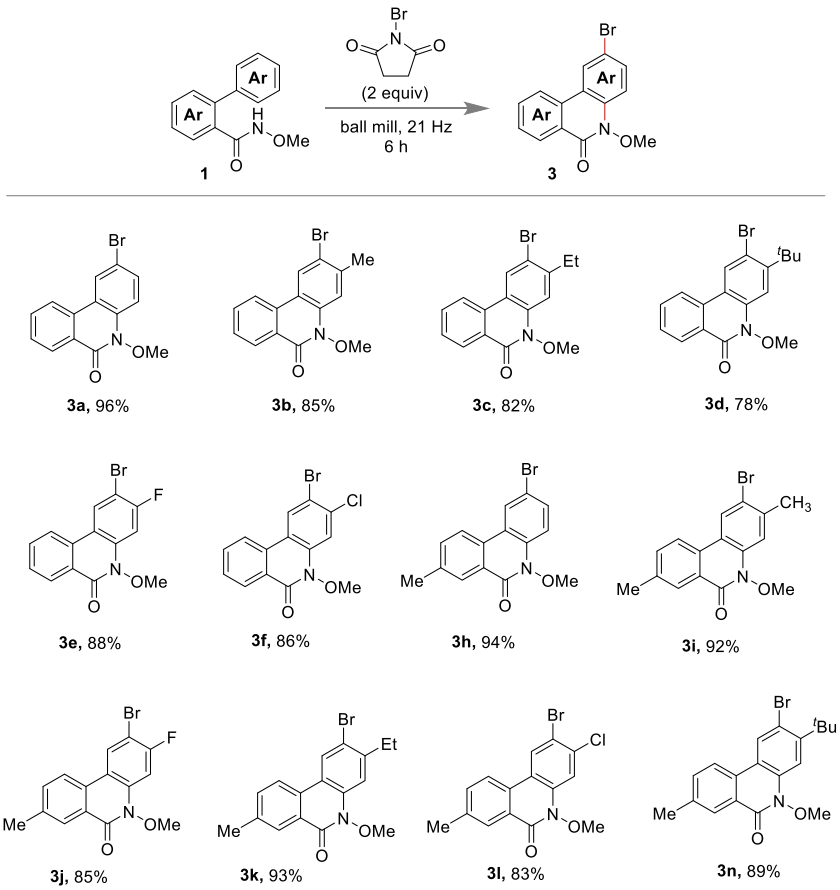

Figure 2. Substrate scope for the NBS-mediated cascaded cyclization and bromination reaction.

zamide with arynes,[44,51] Pd-nanoparticle-catalyzed C−H activation reaction,[52] deaminative synthesis from aniline via activation of C−H bonds,[53] oxidative insertion of CO to *o*-arylanilines,[54] and *N*-sulfonyl-2-aminobiaryls,[55] Pd-catalyzed aryne multicomponent reaction,[56] etc. Xue and co-workers reported the synthesis of 2-substituted phenanthridinones from *N*-methoxybenzamides via a sequential one-pot synthesis using tetrabutylammonium bromide and a PhI−peracid combination (Figure 1b).[57] Again, Xue and co-workers reported phenanthridinone synthesis using PhI−*m*CPBA-mediated oxidative C−N coupling (Figure 1b).[58] The mechanochemical synthesis of phenanthridinone or their halogenated derivatives is shown in Figure 1c (this work). During the reactions, NBS and NCS initially assisted an oxidative C−N coupling reaction followed by a halogenation reaction. Therefore, the bifunctionality of the reagents NBS and NCS was established. However, NIS led to the oxidative C−N coupling reaction,[59] and no halogenation was observed (Figure 1c).

RESULTS AND DISCUSSION

During optimization of the reaction conditions (Table 1), *N*-methoxy[1,1′-biphenyl]-2-carboxamide (**1a**) was used as the model substrate under mechanochemical ball-milling conditions (21 Hz) for 6 h to monitor the formation of unsubstituted (**2a**), bromo- (**3a**), or chlorophenanthridinones (**4a**). The ratios of the products were determined using ^{1}H NMR spectroscopy. Using 1.0 equiv of NBS, an inseparable mixture of the nonbrominated (**2a**) and brominated (**3a**) phenanthridinones in a ratio of 1:3 was obtained with 53% overall yield (entry 1). However, the ratio was changed to 1:10 with 1.5 equiv of NBS, and the overall yield was increased to 73% (entry 2). Compound **3a** obtained with 96% yield when 2.0 equiv of the NBS was used (entry 3). A similar trend was observed using NCS (entries 4 and 5) and the corresponding products were obtained with 51% and 94% overall yields. On the other hand, NIS led to 5-methoxyphenanthridin-6(5*H*)-one (**2a**) in up to 97% yields (entries 6−8). The iodine(III) reagents PIDA and PIFA led to **2a** with 60% and 54% yield, respectively (entries 9 and 10). No product was detected when oxidants like $NH_4S_2O_8$−TBAI (entry 11), $K_2S_2O_8$−TBAI (entry 12), or molecular iodines (entry 13) were used. The yield of product **2a** was not encouraging when the oxidants DDQ (entry 14) and Oxone (entry 15) were used. Furthermore, the yield of expected product (**2a**) decreased with the lowering of the operating frequency from 21 to 16 Hz (entry 16). On the other hand, the desired product (**2a**) yield was unaltered with increasing the operating frequency from 21 to 25 Hz (entry 17). Interestingly, the selective bromination and chlorination took place at the para-position with respect to the newly formed C−N bond. The halogenation reaction was inhibited when the 3′-position of the starting compounds (i.e., the para position with respect to the newly formed C−N bond) had a substituent, and only cyclization reactions were preferable. In this context, substitutions at the meta position of phenyl ring linked with *N*-methoxybenzamide (**1m** and **1o**, Supporting Information) were unable to deliver the halogenated phenanthridinones.

The substrate scope for the NBS-mediated cyclization followed by a bromination reaction is shown in Figure 2. When *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (**1a**) was treated with 2.0 equiv of NBS, 2-bromo-5-methoxyphenan-

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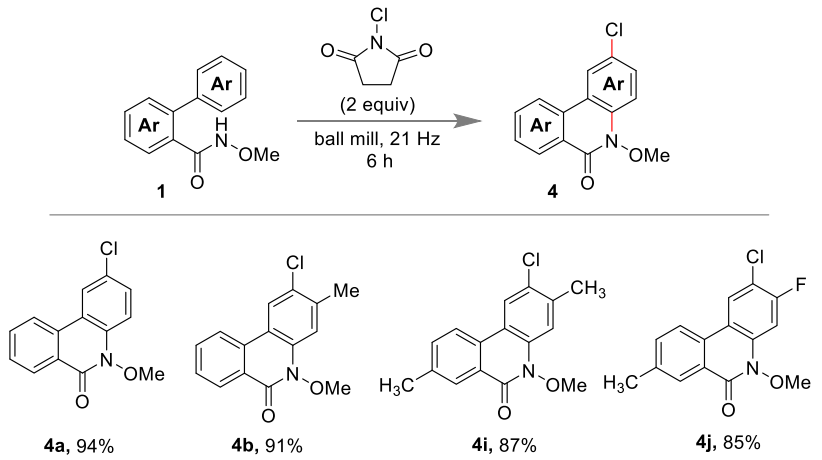

Figure 3. Substrate scope for the NCS-mediated reaction.

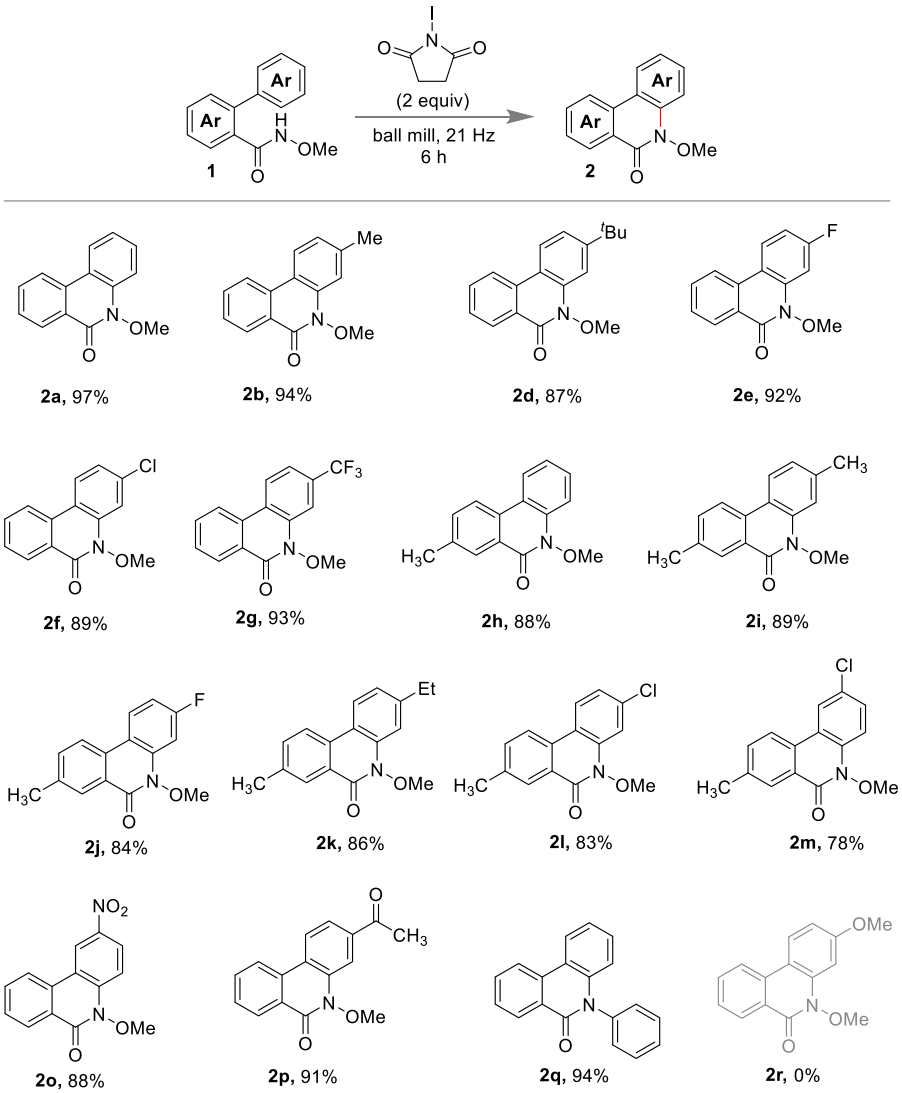

Figure 4. Substrate scope for the cyclization reaction using NIS.

thridin-6(5*H*)-one (**3a**) was obtained and the yield was 96%. The methyl-, ethyl-, and *tert*-butyl-substituted phenyl ring attached to *N*-methoxybenzamide groups led to **3b**, **3c**, and **3d**, respectively, in good yields. The X-ray structure of **3c** (CCDC 2074176) is shown in the Supporting Information. Similarly, fluoro- and chloro-substituted derivatives resulted in **3e** and **3f** with 88% and 86% yields, respectively. The alkyl substitution at the *N*-methoxybenzamide also resulted in good yields of the products (up to 94%). The phenyl ring containing fluoro and chloro groups led to the corresponding phenanthridinones in

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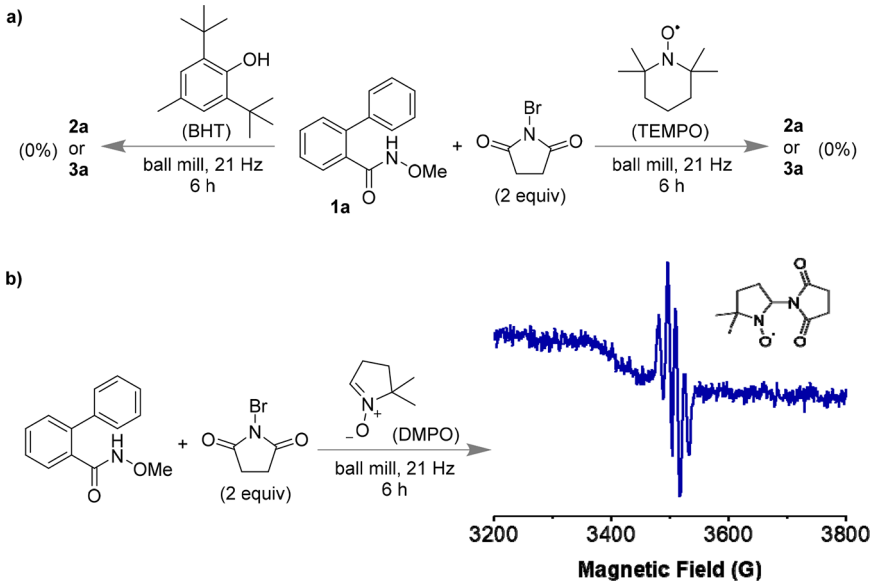

Figure 5. Control experiments. (a) Experiments with BHT and TEMPO. (b) EPR experiment using DMPO under standard conditions and the corresponding spectrum.

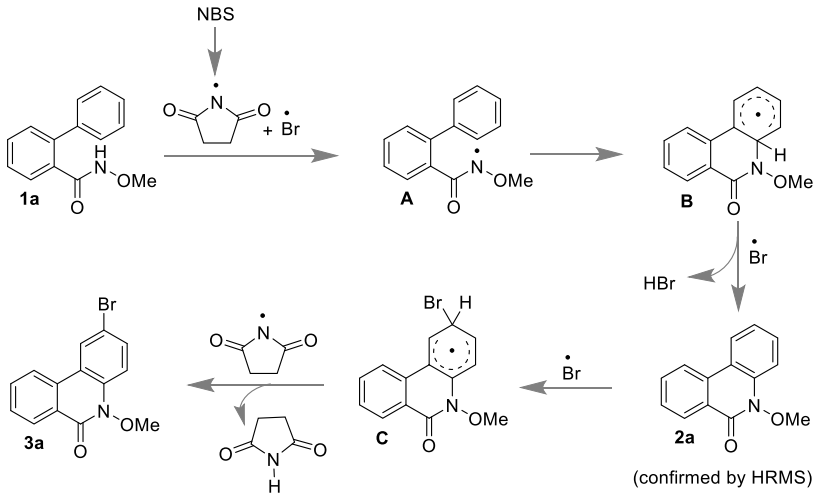

Figure 6. Plausible mechanism for the NBS-mediated reaction.

good yields. Similarly, various alkyl substitutions at the phenyl rings of methyl-substituted *N*-methoxybenzamide yielded the corresponding products in high yields.

The NCS-mediated cascaded cyclization and chlorination reactions were performed using 2.0 equiv of NCS (Figure 3). Compound **4a** was obtained with 94% yield, and the structure was confirmed by X-ray crystallography (CCDC 2074177, Supporting Information). The substrates **1b** and **1i** could be transformed into the expected products **4b** and **4i** with 91% and 87% yields, respectively. However, the phenyl ring containing fluoro group of methyl-substituted *N*-methoxybenzamide (**1j**) afforded the desire phenanthridinones (**4j**) with 85% yields. Similarly, various alkyl substitutions at the phenyl rings of methyl-substituted *N*-methoxybenzamide yielded the corresponding products in high yields.

The substrate scope for the synthesis of phenanthridinones **2** using NIS is shown in Figure 4. For example, 5-methoxyphenanthridin-6(5*H*)-one (**2a**) was obtained with 97% yield. Different substitutions at the phenyl ring linked with *N*-methoxybenzamide played a crucial role in the reaction yields. Methyl- and *tert*-butyl-substituted derivatives **2b** and **2d** were obtained in yields of 94% and 87%, respectively. The structure of **2b** was confirmed by X-ray crystallography (CCDC 2074179, Supporting Information). A structure identical to that of compound **2b** has also been reported previously.[52] Similarly, electron-withdrawing substitutions such as fluoro, chloro, and trifluoromethyl also resulted in the corresponding compounds **2e**, **2f**, and **2g** with good yields. Again, the methyl-substituted *N*-methoxybenzamide derivatives also led to the corresponding cyclized products efficiently. The yield of **2h** was 88%. Likewise, the phenyl group having methyl, fluoro, ethyl, and chloro substitution afforded the corresponding products **2i**, **2j**, **2k**, and **2l** in moderate yields (up to 86%). Notably, the incorporation of a chloro group at the *meta* position of the phenyl ring linked with methyl-substituted *N*-methoxybenzamide was converted to the desired product **2m** with a 78% yield. Similarly, a nitro group at the *meta* position of the phenyl ring linked with *N*-methoxybenzamide led to cyclized product **2o** with 88% yield. Again, having an electron-withdrawing −COMe group at the aromatic ring (**1p**) was successfully converted to **2p**

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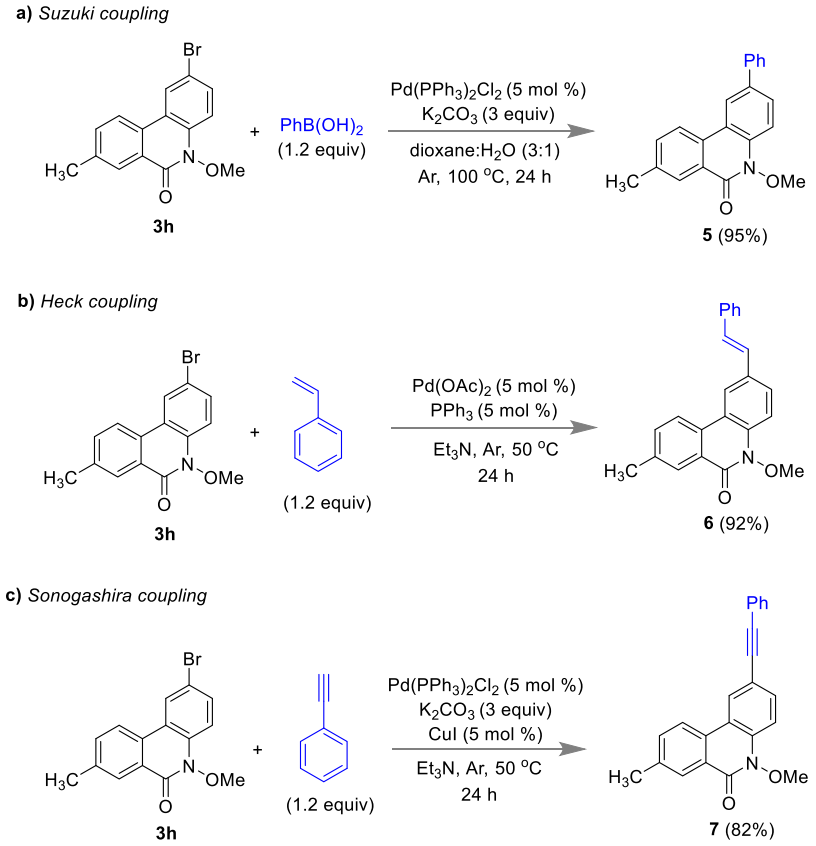

Figure 7. Synthetic applications of **3h**.

with 91% yield. The replacement of the methoxy group with the phenyl group of biphenyl benzamide (**1q**) also afforded the corresponding product (**2q**) with 94% yield. Unfortunately, methoxy (−OMe) substituted phenyl rings attached to an *N*-methoxybenzamide group and (C═O)NH-Me group on the aromatic rings failed to provide the desired products. Furthermore, we have shown the calculation of the environmental impact factor (E_{mw}) or *E*-factor based on the molecular weight (Table S4, Supporting Information). The *E*-factor calculation reveals that this mechanochemical method is superior to the existing methods.[60]

The substrates **1o**−**1r** was unsuccessful to afford the halogenated phenanthridinones using NBS and NCS under standard reaction condition (Chart S1, Supporting Information).

Control experiments shown in Figure 5, helped to understand the mechanism of the reaction. The radical trapping experiment using BHT (butylated hydroxytoluene) and TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) supported a radical-induced mechanism (Figure 5a). The EPR experiments also endorsed for the radical-based mechanism since an EPR signal was observed when a free-radical spin-trapping reagent DMPO (5,5-dimethyl-1-pyrroline *N*-oxide)[61] was used under the optimized reaction conditions (Figure 5b). The DMPO adduct was also identified by LCMS study (Supporting Information).

On the basis of the control experiments and a literature report,[62] a plausible mechanism for the NBS-mediated reaction is proposed in Figure 6. It was expected that NCS also followed a similar pathway for the formation of **4a** via **2a**. First, *N*-bromosuccinimide underwent a homolytic cleavage to form succinimide and bromine radical. Next, **1a** reacted with succinimide to produce the intermediate **A**, which underwent an intramolecular cyclization to form another intermediate **B**. The intermediate **B** was aromatized by the bromine radical to form the cyclized product **2a** (confirmed by HRMS). The compound **2a** was further brominated to **3a** in the presence of bromine radical via the intermediate **C**. Using NIS, the cyclized product **2a** was obtained as the final product because, under mechanochemical conditions, halogenation using NIS could be possible only for the electron-rich substrates.[63]

The synthetic utility of the methodology is shown in Figure 7 using 2-bromo-5-methoxy-8-methylphenanthridin-6(5*H*)-one (**3h**). The Suzuki coupling reaction between **3h** and phenyl boronic acid led to **5** with 95% yields (Figure 7a). The treatment of **3h** with styrene afforded compound **6** in 92% yields via Heck coupling (Figure 7b). In addition, the Sonogashira coupling of 2-bromo-5-methoxy-8-methylphenanthridin-6(5*H*)-one **3h** and phenylacetylene in the presence of $Pd(PPh_3)_2Cl_2$ using CuI gave 5-methoxy-8-methyl-2-(phenylethynyl)phenanthridin-6(5*H*)-one **7** in 82% yield (Figure 7c).

Furthermore, we have performed a large-scale synthesis using *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (**1a**) as the starting material (Figure 8). Under the standard reaction conditions, when *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (**1a**) was treated with appropriate proportions of NBS (for **3a**, Figure 8a) and NIS (for **2a**, Figure 8b), the corresponding phenanthridinones **3a** and **2a** were isolated with 94% and 96% yields, respectively.

Nitrogen-based heterocyclic compounds containing carbonyl groups in their molecular skeleton show n-π^* and π−π^* electronic transitions. We have also examined the photophysical behavior[64,65] of the phenanthridinone derivatives. The UV−vis and fluorescence spectra of the phenanthridinone derivatives were recorded in dichloromethane solvent at $\lambda_{ex} \sim 240$ nm

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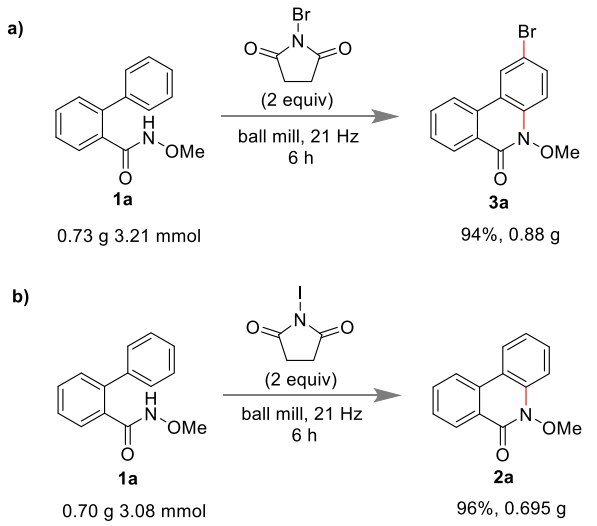

Figure 8. Large-scale synthesis of (a) **3a** and (b) **2a**.

(Supporting Information). Interestingly, the second λ_{em} of the selected phenanthridinones appeared at ~500 nm. We anticipate that these dual emission properties of the phenanthridinone derivatives might be useful in materials chemistry.[65,66]

CONCLUSION

In summary, we have developed a solvent-free mechanochemical method for a cascaded oxidative C−N bond coupling and followed by a halogenation reaction using *N*-bromosuccinimides (NBS) and *N*-chlorosuccinimide (NCS) as bifunctional reagents for the synthesis of phenanthridinones. The NBS and NCS first assisted the oxidative C−N coupling and subsequent halogenation reactions. However, only oxidative intramolecular C−N coupling was observed for the reactions using *N*-iodosuccinimide (NIS). All of the reactions were highly efficient and worked under metal-free and mild conditions. The results from radical-trapping experiments with BHT, TEMPO and the EPR experiment using DMPO helped mechanistically establish that the reaction proceeded via a radical pathway. In addition, the calculation of the environmental impact factor (*E*-factor) also helped to rationalize that the current approach is superior to the existing methods. Again, the dual emissive nature of the phenanthridinone derivatives reveal that these synthesized compounds might be useful for materials applications.

EXPERIMENTAL SECTION

General Information. Commercially available reagents and solvents were used as received. Column chromatographic purifications of the compounds were performed using silica gel (mesh 230−400, 100−200) and hexane−ethyl acetate solvent mixtures. NMR spectra were recorded on 400 or 700 MHz instruments at 25 °C. The chemical shift values are reported in parts per million (ppm) concerning residual trichloromethane (7.26 ppm for ^{1}H and 77.16 ppm for ^{13}C). The peak patterns are designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; td: triplet of doublets; brs: broad singlet. The coupling constants (*J*) are reported in hertz (Hz). High-resolution mass spectra (HR-MS) were recorded on an ESI-TOF (time-of-flight) mass spectrometer. Infrared (IR) spectral data are reported in wavenumbers (cm^{-1}). The mechanochemical experiments were performed in a Mixer Mill MM 200, which has a maximum operating frequency of up to 25 Hz. For the optimization of the reaction conditions and substrate scope, a 10 mL milling jar with one grinding ball (15 mm diameter, stainless steel) was used. However, for the large-scale synthesis, a 25 mL milling jar with one grinding ball (15 mm diameter, stainless steel) was used. For every milling procedure after 90 min the instrument was stopped and allowed to sit for 15 min. The resting time is not included during the calculation of the reaction time. The reactions were performed in a well-ventilated fume hood to avoid excessive heating of the jars during the milling process. The software used for NMR analysis was MestreNova, and for UV−vis and fluorescence it was origin pro 2015. UV−vis spectra were recorded on a JASCO V-730 UV−vis spectrometer, and emission spectral studies were measured using a PerkinElmer LS 55spectrophotometer with an optical cell of 1 cm path length. FT-IR spectra were recorded after a thin layer of the compounds was placed on the surface of the NaCl crystal using dichloromethane. Melting points of the compounds were determined using a digital melting point apparatus and are uncorrected.

General Procedure for the Preparation of *N*-Methoxy-[1,1′-biphenyl]-2-carboxamide (1a)[58] Followed by 2−4. Figure 9 details the synthesis of compounds **1a**−**4a**.

Synthesis of Methyl 2-Iodobenzoate. In an oven-dried 100 mL round-bottom flask equipped with a stir-bar were added 2-iodobenzoic acid (10 mmol, 2.5 g) and 30 mL of MeOH. Concentrated sulfuric acid

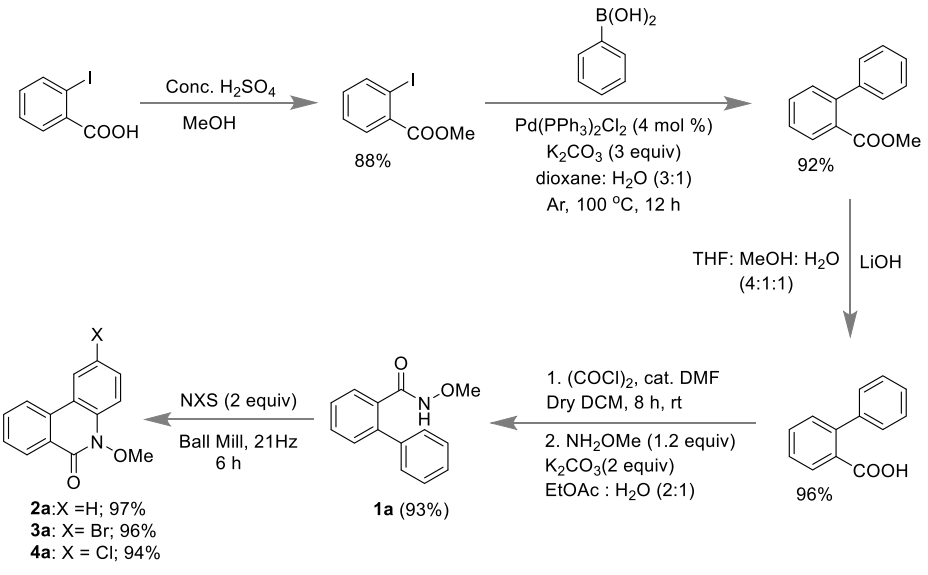

Figure 9. Synthesis of *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (**1a**) followed by **2a**, **3a**, and **4a**.

https://doi.org/10.1021/acs.joc.1c01742
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(2 mL) was added slowly to the reaction mixture and refluxed at 80 °C for 8 h. After completion of the reaction, the round-bottom flask was cooled to room temperature, and excess MeOH was evaporated. Then the reaction mixture was washed with saturated $NaHCO_3$ (aq) solution and ethyl acetate (2 × 25 mL). The organic layer was collected and concentrated under vacuum to give a colorless liquid, which was directly used in the next step.

Synthesis of Methyl [1,1′-Biphenyl]-2-carboxylate. A solution of substituted 2-halogenated methyl benzoate (2 mmol), aryl boronic acid (3 mmol, 1.5 equiv), $Pd(PPh_3)_2Cl_2$ (0.08 mmol, 0.04 equiv), and potassium carbonate (6 mmol, 3 equiv) in dioxane/H_2O (6 mL/2 mL) was stirred at 100 °C under an argon atmosphere until the starting material was completely consumed (typically 12 h). The reaction mixture was diluted with brine (25 mL) and extracted with EtOAc (25 mL × 2). Then the combined organic layers were dried over Na_2SO_4, and 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.

Synthesis of [1,1′-Biphenyl]-2-carboxylic Acid. A mixture of methyl [1,1′-biphenyl]-2-carboxylate (3.95 mmol, 1.0 equiv) and LiOH (11.8 mmol, 3.0 equiv) was taken in a mixed solvent of THF/MeOH/H_2O in a 4:1:1 ratio. Then the reaction mixture was heated at 70 °C for 8 h. After being cooled to room temperature, the reaction mixture was concentrated under vacuum and adjusted to pH ∼ 1 by using 1 N HCl. The mixture was extracted with EtOAc, and the organic layer was dried over Na_2SO_4, filtered, and concentrated in a vacuum. The residue was purified by column chromatography to give the product (96% as a white solid).

Synthesis of N-Methoxy-[1,1′-biphenyl]-2-carboxamide ***1****.* To a solution of [1,1′-biphenyl]-2-carboxylic acid (3.0 mmol, 1.0 equiv) in dry CH_2Cl_2 (10 mL) at 0 °C under argon (Ar) was added dropwise oxalyl chloride (0.34 mL, 3.6 mmol, 1.2 equiv) followed by a catalytic amount of dry DMF (2 drops). The reaction mixture was allowed to stir at room temperature until completion (typically 8 h). The solvent was then removed under reduced pressure to afford the corresponding crude acyl chloride and proceeded to the next step without any further purification.

Methoxyamine hydrochloride (3.6 mmol, 1.2 equiv) and K_2CO_3 (6.00 mmol, 2.0 equiv) were added to a biphasic mixture of EtOAc and H_2O in a ratio of 2:1. The resulting solution was cooled to 0 °C followed by dropwise addition of the unpurified acid chloride which was dissolved in a minimum amount of EtOAc. The reaction was allowed to stir at room temperature for 8 h. After that, the organic phases were extracted with EtOAc (3 × 30 mL) and dried over $MgSO_4$. The solvent was concentrated under vacuum, and the crude product was purified by column chromatography to afford *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (93%).

General Procedure for the Synthesis of 5-Methoxyphenanthridin-6(5*H*)-ones 2. In a 10 mL stainless steel milling jar were added *N*-methoxy-[1,1′-biphenyl]-2-carboxamide (60 mg, 0.264 mmol), *N*-halosuccinimide (0.528 mmol, 2 equiv), and one grinding ball (15 mm diameter, stainless steel). Then the reaction was carried out for 6 h at 21 Hz, and the progress of the reaction was monitored by TLC (thin-layer chromatography). After completion of the reaction, the mixture was dissolved in 15 mL (3 × 5 mL) of dichloromethane (DCM), and the resulting solution was evaporated to dryness. The crude residue was purified on silica gel column chromatography (20% EtOAc in hexane) to get the products.

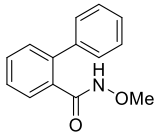
Procedure for Large-Scale Synthesis. *N*-Methoxy-[1,1′-biphenyl]-2-carboxamide (**1a**) (3 mmol) and appropriate proportions of NBS (for **3a**) and NIS (for **2a**) were taken in a 25 mL stainless steel milling jar containing one grinding ball (15 mm diameter, stainless steel). The reaction mixer was milled for 6 h for complete conversion. Then the reaction mixture was extracted with dichloromethane (DCM), and the crude product was purified by flash chromatography to obtain **3a** and **2a** with 94% and 96% yield, respectively.

*Synthesis of 5-Methoxy-8-methyl-2-phenylphenanthridin-6(5H)-one (****5****).* A 15 mL sealed tube containing a magnetic bar was charged with 2-bromo-5-methoxy-8-methylphenanthridin-6(5*H*)-one (0.25 mmol, 1.0 equiv), phenyl boronic acid (0.32 mmol, 1.3 equiv), K_2CO_3 (0.75 mmol, 3.0 equiv), and $Pd(PPh_3)_2Cl_2$ (0.01 mmol, 9 mg) in dioxane/H_2O (6 mL/2 mL) under an argon atmosphere. Then the reaction mixture was placed into a preheated oil bath at 100 °C for 24 h. The reaction mixture was cooled to room temperature, diluted with brine (25 mL), and extracted with EtOAc (25 mL × 2). The layers were separated, and the aqueous layer was extracted with 2 × 8 mL of ethyl acetate. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuum. The crude product was purified by column chromatography to afford 5-methoxy-8-methyl-2-phenylphenanthridin-6(5*H*)-one (**5**) with 95% yield.

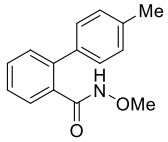
*Synthesis of (E)-5-Methoxy-8-methyl-2-styrylphenanthridin-6(5H)-one (****6****).* 2-Bromo-5-methoxy-8-methylphenanthridin-6(5*H*)-one (0.18 mmol, 1.0 equiv), styrene (0.22 mmol, 1.2 equiv), PPh_3 (0.013 mmol, 4 mg), and $Pd(OAc)_2$ (5 mol %, 23 mg) in triethylamine (6 mL) were placed in a 15 mL sealed tube under an argon atmosphere. Then the reaction mixture was stirred into a preheated oil bath at 100 °C for 12 h. After the mixture was cooled to room temperature, the solvent was evaporated to dryness. Then brine water and ethyl acetate were added to the reaction mixture. The combined organic extracts were dried over anhydrous Na_2SO_4, and the solvent was evaporated. The resulting residue was purified by column chromatography to produce (*E*)-5-methoxy-8-methyl-2-styrylphenanthridin-6(5*H*)-one (**6**) with 92% yield.

*Synthesis of 5-Methoxy-8-methyl-2-(phenylethynyl)-phenanthridin-6(5H)-one (****7****).* A 15 mL sealed tube equipped with a magnetic stirring bar was charged with 2-bromo-5-methoxy-8-methylphenanthridin-6(5*H*)-one (0.18 mmol, 1.0 equiv), phenylacetylene (0.20 mmol, 1.1 equiv), CuI (5 mol %, 2 mg), and $Pd(PPh_3)_2Cl_2$ (5 mol %, 7 mg) in triethyl amine (6 mL) under an argon atmosphere. Then reaction mixture was stirred into a preheated oil bath at 50 °C for 24 h. The mixture was cooled to room temperature, and solvent was evaporated to dryness. Then reaction mixture was diluted with brine solution and ethyl acetate (15 mL × 2). Then the organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuum. The crude product was then purified by flash chromatography to afford 5-methoxy-8-methyl-2-(phenylethynyl)phenanthridin-6(5*H*)-one (**7**) with 82% yield.

*N-Methoxy-[1,1′-biphenyl]-2-carboxamide (****1a****):*[57] R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 93% (533 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.64 (d, J = 6.8 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.44−7.40 (m, 5H), 7.40−7.36 (m, 2H), 3.51 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.5, 140.0, 139.7, 132.3, 130.9, 130.2, 129.3, 128.9, 128.8, 128.2, 127.8, 64.1; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{14}NO_2$ $[M + H]^+$ 228.1019, found 228.1023.



*N-Methoxy-4′-methyl-[1,1′-biphenyl]-2-carboxamide (****1b****):*[58] R_f = 0.45 (hexane/ethyl acetate 7:3); white solid; yield 97% (576 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.66 (s, 1H), 7.51 (t, J = 7.2 Hz, 1H), 7.44−7.36 (m, 2H), 7.33 (d, J = 7.6 Hz, 2H), 7.26 (t, J = 7.2 Hz, 2H), 3.58 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.7, 139.9, 138.1, 136.7, 132.2, 130.9, 130.2, 129.6, 129.4, 128.7, 127.6, 64.1, 21.3; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{16}NO_2$ $[M + H]^+$ 242.1176, found 242.1179.



*4′-Ethyl-N-methoxy-[1,1′-biphenyl]-2-carboxamide (****1c****):* R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 91% (453 mg); mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.50 (td, J = 7.6, 1.2 Hz, 1H), 7.39 (dd, J = 6.4, 1.2 Hz, 2H), 7.37−7.33 (m, 2H), 7.30−7.25 (m, 2H), 3.55 (s, 3H), 2.71 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.7, 144.5, 140.1, 137.1, 132.4, 130.8, 130.2, 129.4, 128.8,

https://doi.org/10.1021/acs.joc.1c01742
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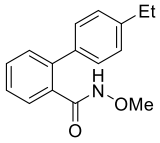
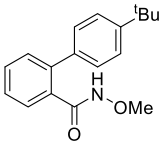
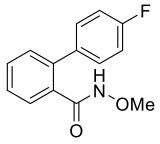
128.4, 127.6, 64.0, 28.7, 15.6; IR (KBr) $\tilde{\nu}$ = 3169, 2964, 2917, 2848, 1651, 1537, 1492, 1456, 1438, 1301, 1158, 1041, 1029, 839 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{17}NO_2Na$ $[M + Na]^+$ 278.1151, found 278.1150.



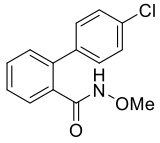
*4′-tert-Butyl-N-methoxy-[1,1′-biphenyl]-2-carboxamide (**1d**):* R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 94% (670 mg); mp 128−130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.65 (d, J = 6.8 Hz, 1H), 7.52−7.42 (m, 3H), 7.42−7.30 (m, 4H), 3.50 (s, 3H), 1.34 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.6, 151.3, 139.9, 136.7, 132.3, 130.9, 130.2, 129.3, 128.5, 127.6, 125.8, 63.9, 34.7, 31.4; IR (KBr) $\tilde{\nu}$ = 3157, 2959, 2900, 2862, 1659, 1638, 1513, 1477, 1458, 1439, 1307, 1268, 1029, 886 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{18}H_{21}NO_2Na$ $[M + Na]^+$ 306.1465, found 306.1459.



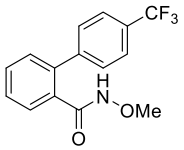
*4′-Fluoro-N-methoxy-[1,1′-biphenyl]-2-carboxamide (**1e**):*[58] R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 87% (585 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.59 (d, J = 5.2 Hz, 1H), 7.50 (tt, J = 7.6, 1.6 Hz, 1H), 7.45−7.37 (m, 3H), 7.37−7.33 (m, 1H), 7.15−7.07 (m, 2H), 3.58 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.5, 162.8 (d, J = 247.9 Hz), 139.1, 135.7, 132.4, 130.9, 130.5 (d, J = 8.1 Hz), 130.2, 129.2, 127.9, 115.8 (d, J = 21.5 Hz), 64.2; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{12}FNO_2Na$ $[M + Na]^+$ 268.0744, found 268.0735.



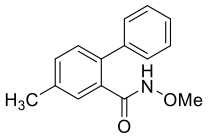
*4′-Chloro-N-methoxy-[1,1′-biphenyl]-2-carboxamide (**1f**):*[58] R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 90% (580 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.57 (d, J = 6.8 Hz, 1H), 7.50 (t, J = 7.2 Hz, 1H), 7.45−7.37 (m, 3H), 7.37−7.29 (m, 3H), 3.57 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.4, 138.9, 138.2, 134.3, 132.4, 130.9, 130.2, 130.1, 129.1, 128.9, 128.0, 64.1; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{12}ClNO_2Na$ $[M + Na]^+$ 284.0449, found 284.0440.



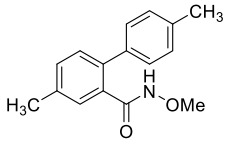
*N-Methoxy-4′-(trifluoromethyl)-[1,1′-biphenyl]-2-carboxamide (**1g**):*[58] R_f = 0.45 (hexane/ethyl acetate 7:3); white solid; yield 94% (557 mg); ^1H NMR (700 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.69−7.62 (m, 2H), 7.58−7.47 (m, 4H), 7.46−7.32 (m, 2H), 3.51 (s, 3H); $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 167.1, 143.5, 139.0, 132.5, 131.0, 130.3, 129.2, 128.9, 128.4, 125.6, 124.2 (q, J = 272.2 Hz), 64.0; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{12}F_3NO_2Na$ $[M + Na]^+$ 318.0712, found 318.0726.



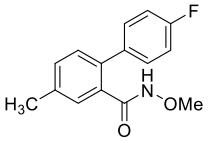
*N-Methoxy-4-methyl-[1,1′-biphenyl]-2-carboxamide (**1h**):*[57] R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 90% (404 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.49 (s, 1H), 7.44−7.40 (m, 4H), 7.40−7.36 (m, 1H), 7.31−7.27 (m, 2H), 3.53 (s, 3H), 2.41 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) 167.7, 139.7, 137.9, 137.2, 132.1, 131.7, 130.1, 129.9, 128.9, 128.9, 128.0, 64.1, 21.1; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{15}NO_2Na$ $[M + Na]^+$ 264.0995, found 264.0990.



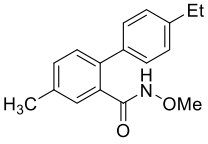
*N-Methoxy-4,4′-dimethyl-[1,1′-biphenyl]-2-carboxamide (**1i**):* R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 88% (415 mg); mp 135−137 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.48 (s, 1H), 7.29 (d, J = 7.2 Hz, 3H), 7.26−7.19 (m, 3H), 3.57 (s, 3H), 2.39 (s, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.0, 137.9, 137.6, 137.1, 136.7, 131.9, 131.7, 130.2, 129.9, 129.6, 128.7, 64.1, 21.3, 21.0; IR (KBr) $\tilde{\nu}$ = 3155, 3021, 2918, 2851, 1659, 1606, 1466, 1439, 1416, 1294, 1036, 943 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{18}NO_2$ $[M + H]^+$ 256.1332, found 256.1331.



*4′-Fluoro-N-methoxy-4-methyl-[1,1′-biphenyl]-2-carboxamide (**1j**):* R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 97% (475 mg); mp 154−156 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.41 (s, 1H), 7.36 (dd, J = 8.0, 5.6 Hz, 2H), 7.30 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 7.2 Hz, 1H), 7.09 (t, J = 8.4 Hz, 2H), 3.57 (s, 3H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.6, 162.7 (d, J = 247.5 Hz), 137.9, 136.1, 135.7, 132.1, 131.7, 130.4 (d, J = 8.1 Hz), 130.1, 129.7, 115.8 (d, J = 21.5 Hz), 64.1, 21.0; IR (KBr) $\tilde{\nu}$ = 3112, 2917, 2820, 1641, 1601, 1510, 1488, 1442, 1313, 1219, 1158, 1036, 948, 849 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{15}FNO_2$ $[M + H]^+$ 260.1081, found 260.1085.



*4′-Ethyl-N-methoxy-4-methyl-[1,1′-biphenyl]-2-carboxamide (**1k**):* R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 98% (474 mg); mp 128−130 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.51 (s, 1H), 7.36−7.31 (m, 3H), 7.30−7.26 (m, 3H), 3.57 (s, 3H), 2.70 (q, J = 7.6 Hz, 2H), 2.42 (s, 3H), 1.28 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.0, 144.3, 137.6, 137.1, 136.9, 131.8, 131.8, 130.1, 129.9, 128.8, 128.4, 28.7, 21.1, 15.7; IR (KBr) $\tilde{\nu}$ = 3130, 2959, 2929, 2865, 1659, 1637, 1507, 1481, 1436, 1316, 1147, 1040, 945, 846 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{17}H_{19}NO_2Na$ $[M + Na]^+$ 292.1308, found 292.1321.



*4′-Chloro-N-methoxy-4-methyl-[1,1′-biphenyl]-2-carboxamide (**1l**):* R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 94% (329 mg); mp 151−153 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.47−7.40 (m, 2H), 7.40−7.35 (m, 3H), 7.33 (s, 1H), 7.28 (t, J = 6.4 Hz, 1H), 3.62 (s, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.5, 138.2, 138.1, 136.1, 134.1, 132.1, 131.8, 130.1 (×2), 129.7, 128.9, 64.2, 21.1; IR (KBr) $\tilde{\nu}$ = 3204, 2921, 2852, 1648, 1509, 1473, 1312, 1121, 1093, 1050, 1016, 838, 810 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{14}ClNO_2Na$ $[M + Na]^+$ 298.0605, found 298.0614.

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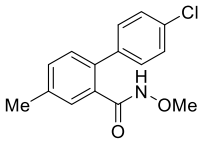
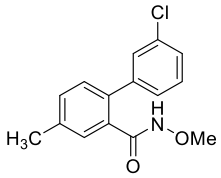
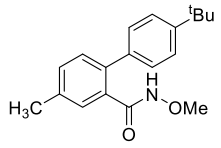


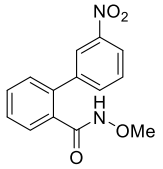
3′-Chloro-N-methoxy-4-methyl-[1,1′-biphenyl]-2-carboxamide (***1m***): R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 98% (478 mg); mp 126−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.42 (s, 2H), 7.36−7.34 (m, 2H), 7.34−7.30 (m, 2H), 7.27 (d, J = 8.0 Hz, 1H), 3.59 (s, 3H), 2.42 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.2, 141.5, 138.4, 135.8, 134.6, 132.2, 131.7, 130.0, 129.7, 128.8, 127.9, 127.1, 64.1, 21.1; IR (KBr) $\tilde{\nu}$ = 3127, 2970, 2923, 1629, 1595, 1523, 1465, 1436, 1318, 1120, 1046, 930, 820 cm^{-1};HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{14}ClNO_2Na$ $[M + Na]^+$ 298.0605, found 298.0621.



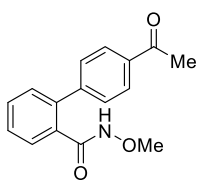
4′-tert-Butyl-N-methoxy-4-methyl-[1,1′-biphenyl]-2-carboxamide (***1n***): R_f = 0.50 (hexane/ethyl acetate 7:3); white solid; yield 96% (530 mg); mp 112−114 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.57 (s, 1H), 7.52 (s, 1H), 7.51 (s, 1H), 7.42 (s, 1H), 7.41 (s, 1H), 7.38 (d, J = 7.7 Hz, 1H), 7.35 (d, J = 8.4 Hz, 1H), 3.59 (s, 3H), 2.48 (s, 3H), 1.42 (s, 9H); ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 167.8, 151.1, 137.6, 137.1, 136.7, 132.1, 131.7, 130.1, 129.9, 128.5, 125.8, 63.9, 34.7, 31.5, 21.1; IR (KBr) $\tilde{\nu}$ = 3215, 2960, 1654, 1478, 1393, 1297, 1203, 1034, 928, 814 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{19}H_{23}NO_2Na$ $[M + Na]^+$ 320.1621, found 320.1638.



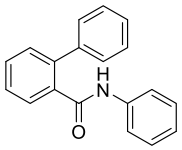
N-Methoxy-3′-nitro-[1,1′-biphenyl]-2-carboxamide (***1o***): R_f = 0.45 (hexane/ethyl acetate 7:3); white solid; yield 93% (257 mg); mp 176−177 °C; ^{1}H NMR (400 MHz, $CDCl_{3+}$ TFA-D) δ 8.20 (d, J = 7.2 Hz, 2H), 7.70 (s, 1H), 7.59 (t, J = 7.2 Hz, 2H), 7.52 (s, 1H), 7.49−7.40 (m, 2H), 3.58 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_{3+}$ TFA-D) δ 168.7, 148.3, 140.9, 138.4, 135.1, 132.2, 130.7, 130.4, 130.0, 128.9, 128.8, 123.5, 123.1, 64.5; IR (KBr) $\tilde{\nu}$ = 3134, 2933, 2846, 1654, 1632, 1526, 1497, 1350, 1313, 1036, 939, 762 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{12}N_2O_4Na$ $[M + Na]^+$ 295.0689, found 295.0678.



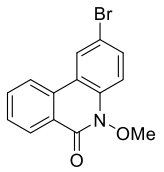
4′-Acetyl-N-methoxy-[1,1′-biphenyl]-2-carboxamide (***1p***): R_f = 0.45 (hexane/ethyl acetate 7:3); white solid; yield 78% (380 mg); mp 153−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51−8.22 (brs, 1H), 8.11−7.85 (m, 2H), 7.64−7.47 (m, 4H), 7.45−7.34 (m, 2H), 3.57 (s, 3H), 2.59 (s, 3H); ^{13}C{^{1}H} (100 MHz, $CDCl_3$) δ 197.8, 167.2, 144.5, 139.1, 136.4, 136.3, 132.5, 130.9, 130.1, 129.0, 128.7, 128.4, 64.1, 26.8; IR (KBr) $\tilde{\nu}$ = 3153, 2974, 1678, 1634, 1576, 1440, 1267, 1032, 1003, 887, 762 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{16}NO_3$ $[M + H]^+$ 270.1125, found 270.1124.



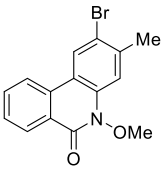
N-Phenyl-[1,1′-biphenyl]-2-carboxamide (***1q***):[67] R_f = 0.50 (hexane/ethyl acetate 4:1); reddish yellow solid; yield 80% (410 mg); mp 103−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.2 Hz, 1H), 7.55 (t, J = 7.2 Hz, 1H), 7.51−7.37 (m, 7H), 7.24 (dd, J = 14.0, 6.4 Hz, 2H), 7.15−7.03 (m, 3H), 6.98 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.3, 140.1, 139.7, 137.7, 135.4, 130.8, 130.5, 129.7, 129.1, 128.9 (×2), 128.2, 128.0, 124.5, 120.1; IR (KBr) $\tilde{\nu}$ = 3331, 2922, 1713, 1662, 1515, 1450, 1131, 1093, 948, 752 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{19}H_{16}NO$ $[M + H]^+$ 274.1226, found 274.1251.



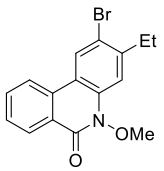
2-Bromo-5-methoxyphenanthridin-6(5H)-one (***3a***):[57] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 96% (74 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.71 (s, 1H), 8.61 (d, J = 8.0 Hz, 1H), 8.34 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.71 (t, J = 7.6 Hz, 1H), 7.59 (d, J = 8.8 Hz, 1H), 4.02 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 155.9, 134.7, 133.3, 132.9, 131.6, 129.1, 127.7, 126.4, 126.0, 123.4, 120.0, 115.9, 114.7, 62.8; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{10}{}^{79}BrNO_2Na$ $[M + Na]^+$ 325.9787, found 325.9789, $C_{14}H_{10}{}^{81}BrNO_2Na$ $[M + Na]^+$ 327.9767, found 327.9776.



2-Bromo-5-methoxy-3-methylphenanthridin-6(5H)-one (***3b***):[57] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 85% (112 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 8.0 Hz, 1H), 8.35 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.6 Hz, 1H), 7.52 (s, 1H), 4.12 (s, 3H), 2.55 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.2, 140.1, 135.0, 132.9, 131.9, 128.7, 128.4, 126.9, 126.3, 121.9, 119.4, 118.2, 114.5, 62.9, 23.6; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{13}{}^{79}BrNO_2$ $[M + H]^+$ 318.0124, found 318.0133, $C_{15}H_{13}{}^{81}BrNO_2$ $[M + H]^+$ 320.0104, found 320.0125.



2-Bromo-3-ethyl-5-methoxyphenanthridin-6(5H)-one (***3c***): R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 82% (106 mg); mp 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 8.0 Hz, 1H), 8.34 (s, 1H), 8.14 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 7.6 Hz, 1H), 7.58 (t, J = 7.6 Hz, 1H), 7.50 (s, 1H), 4.13 (s, 3H), 2.89 (q, J = 7.6 Hz, 2H), 1.32 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.2, 145.5, 135.3, 132.9, 131.9, 128.7, 128.4, 127.3, 126.3, 121.9, 118.7, 118.2, 113.2, 62.9, 29.9, 14.4; IR (KBr) $\tilde{\nu}$ = 2957, 2922, 2851, 1661, 1605, 1495, 1446, 1402, 1326, 1174, 1074, 1051, 1035, 908 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{15}{}^{79}BrNO_2$ $[M + H]^+$ 332.0281, found 332.0262, $C_{16}H_{15}{}^{81}BrNO_2$ $[M + H]^+$ 334.0261, found 320.0246.



2-Bromo-3-tert-butyl-5-methoxyphenanthridin-6(5H)-one (***3d***): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 78% (99 mg); mp 135−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8.0 Hz, 1H), 8.42 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 7.74 (s, 1H), 7.60 (t, J = 7.6 Hz, 1H), 4.14 (s, 3H), 1.61 (s, 9H); ^{13}C{^{1}H}

https://doi.org/10.1021/acs.joc.1c01742
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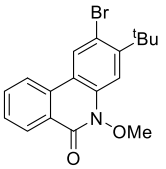
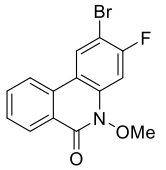
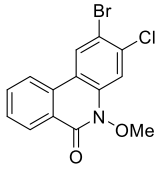
NMR (100 MHz, $CDCl_3$) δ 157.4, 150.1, 134.8, 132.9, 131.7, 130.3, 128.8, 128.5, 126.6, 121.9, 117.9, 116.7, 112.1, 62.9, 37.3, 29.8; IR (KBr) $\tilde{\nu}$ = 2954, 2922, 2852, 1668, 1601, 1465, 1396, 1382, 1315, 1294, 1170, 1048, 1012, 913, 809 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{18}H_{19}{}^{79}BrNO_2$ $[M + H]^+$ 360.0594, found 360.0592, $C_{18}H_{19}{}^{81}BrNO_2$ $[M + H]^+$ 362.0574, found 362.0575.



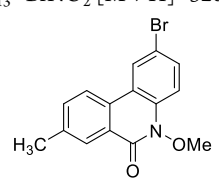
2-Bromo-3-fluoro-5-methoxyphenanthridin-6(5H)-one (***3e***). R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 88% (92 mg); mp 210−212 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.80 (d, J = 7.2 Hz, 1H), 8.53 (d, J = 8.0 Hz, 1H), 8.30 (d, J = 8.0 Hz, 1H), 7.85 (t, J = 7.6 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.60 (d, J = 10.2 Hz, 1H), 4.03 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 158.9 (d, J = 246.3 Hz), 156.1, 136.4 (d, J = 10.2 Hz), 133.3, 131.2, 128.9, 128.7, 127.6, 125.3, 123.3, 116.1, 102.6 (d, J = 22.0 Hz), 100.9 (d, J = 28.8 Hz), 62.9; IR (KBr) $\tilde{\nu}$ = 2915, 2848, 1668, 1644, 1584, 1480, 1447, 1308, 1297, 1277, 1189, 1171, 1057, 1038, 890 cm^{-1};HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{10}{}^{79}BrFNO_2$ $[M + H]^+$ 321.9873, found 321.9868, $C_{14}H_{10}{}^{81}BrFNO_2$ $[M + H]^+$ 323.9854, found 323.9849.



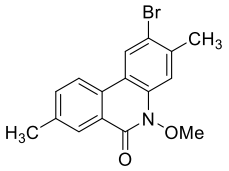
2-Bromo-3-chloro-5-methoxyphenanthridin-6(5H)-one (***3f***):[57] R_f = 0.40 (hexane/ethyl acetate 4:1); white solid; yield 86% (89 mg); ^1H NMR (400 MHz, DMSO- d_6) δ 8.90 (s, 1H), 8.62 (d, J = 8.0 Hz, 1H), 8.34 (d, J = 8.0 Hz, 1H), 7.89 (t, J = 7.6 Hz, 1H), 7.83 (s, 1H), 7.72 (t, J = 7.6 Hz, 1H), 4.04 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO- d_6) δ 156.0, 135.7, 134.7, 133.4, 131.0, 129.3, 128.9, 127.7, 125.9, 123.6, 118.7, 115.6, 113.9, 63.0; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{10}{}^{79}BrClNO_2$ $[M + H]^+$ 337.9578, found 337.9560, $C_{14}H_{10}{}^{81}BrClNO_2$ $[M + H]^+$ 339.9557, found 339.9542.



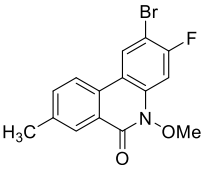
2-Bromo-5-methoxy-8-methylphenanthridin-6(5H)-one (***3h***):[57] R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 94% (62 mg); ^1H NMR (400 MHz, DMSO-d_6) δ 8.61 (d, J = 2.0 Hz, 1H), 8.44 (d, J = 8.4 Hz, 1H), 8.13 (s, 1H), 7.75 (dd, J = 8.8, 2.0 Hz, 1H), 7.67 (dd, J = 8.4, 1.6 Hz, 1H), 7.56 (d, J = 8.8 Hz, 1H), 4.02 (s, 3H), 2.48 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 155.8, 138.9, 134.3, 134.2, 132.3, 128.9, 127.3, 125.9, 125.8, 123.3, 119.9, 115.7, 114.5, 62.7; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{13}{}^{79}BrNO_2$ $[M + H]^+$ 318.0124, found 318.0123, $C_{15}H_{13}{}^{81}BrNO_2$ $[M + H]^+$ 320.0104, found 320.0106.



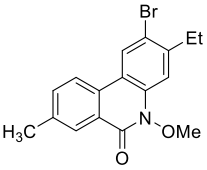
2-Bromo-5-methoxy-3,8-dimethylphenanthridin-6(5H)-one (***3i***): R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 92% (65 mg); mp 168−170 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.27 (d, J = 5.6 Hz, 2H), 8.00 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.46 (s, 1H), 4.07 (s, 3H), 2.50 (s, 3H), 2.47 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 157.2, 139.4, 138.7, 134.5, 134.2, 129.4, 128.3, 126.6, 126.0, 121.9, 119.2, 118.3, 114.3, 62.8, 23.5, 21.4; IR (KBr) $\tilde{\nu}$ = 2954, 2917, 2849, 1729, 1608, 1537, 1492, 1462, 1397, 1207, 1184, 1161, 1079, 1056, 966, 812 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{15}{}^{79}BrNO_2$ $[M + H]^+$ 332.0281, found 332.0265, $C_{16}H_{15}{}^{81}BrNO_2$ $[M + H]^+$ 334.0261, found 334.0246.



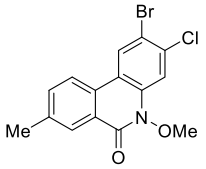
2-Bromo-3-fluoro-5-methoxy-8-methylphenanthridin-6(5H)-one (***3j***): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 85% (88 mg); mp 206−208 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.22 (d, J = 6.8 Hz, 1H), 8.18 (d, J = 0.4 Hz, 1H), 7.88 (d, J = 8.4 Hz, 1H), 7.49 (dd, J = 8.4, 1.6 Hz, 1H), 7.29 (d, J = 9.6 Hz, 1H), 4.04 (s, 3H), 2.43 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 159.3 (d, J = 248.7 Hz), 157.0, 138.9, 135.9 (d, J = 9.7 Hz), 134.3, 128.7, 128.2, 127.9, 125.6, 121.8, 116.2 (d, J = 2.5 Hz), 103.3 (d, J = 22.2 Hz), 100.7 (d, J = 28.7 Hz), 62.9, 21.3; IR (KBr) $\tilde{\nu}$ = 3011, 2948, 2931, 1669, 1607, 1584, 1421, 1397, 1239, 1230, 1187, 1056, 1009, 886, 851 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{12}{}^{79}BrFNO_2$ $[M + H]^+$ 336.0030, found 336.0033, $C_{15}H_{12}{}^{81}BrFNO_2$ $[M + H]^+$ 338.0010, found 338.0013.



2-Bromo-3-ethyl-5-methoxy-8-methylphenanthridin-6(5H)-one (***3k***): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 93% (95 mg); mp 141−143 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.59 (s, 1H), 8.40 (d, J = 8.4 Hz, 1H), 8.10 (s, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.54 (s, 1H), 4.02 (s, 3H), 2.83 (d, J = 7.6 Hz, 2H), 2.47 (s, 3H), 1.25 (t, J = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 155.9, 144.3, 138.5, 134.6, 134.2, 128.9, 127.3, 127.0, 125.5, 123.0, 117.8, 117.8, 113.0, 62.6, 29.1, 20.9, 14.2; IR (KBr) $\tilde{\nu}$ = 2920, 2851, 1729, 1645, 1605, 1462, 1422, 1399, 1336, 1290, 1157, 1049, 1016, 940, 868 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{17}H_{17}{}^{79}BrNO_2$ $[M + H]^+$ 346.0437, found 346.0436, $C_{17}H_{17}{}^{81}BrNO_2$ $[M + H]^+$ 348.0417, found 348.0419.



2-Bromo-3-chloro-5-methoxy-8-methylphenanthridin-6(5H)-one (***3l***): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 83% (85 mg); mp 216−218 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.24 (s, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.66 (s, 1H), 7.55 (d, J = 8.0 Hz, 1H), 4.06 (s, 3H), 2.46 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 156.9, 139.5, 135.3, 135.2, 134.4, 128.6, 128.4, 127.8, 126.2, 122.1, 118.8, 116.3, 114.0, 40.6, 21.4; IR (KBr) $\tilde{\nu}$ = 2920, 2851, 1711, 1672, 1617, 1459, 1389, 1321, 1233, 1221, 1211, 1040, 939, 875 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{12}{}^{79}BrClNO_2$ $[M + H]^+$ 351.9734, found 351.9738, $C_{15}H_{12}{}^{81}BrClNO_2$ $[M + H]^+$ 353.9714, found 353.9719.



2-Bromo-3-tert-butyl-5-methoxy-8-methylphenanthridin-6(5H)-one (***3n***): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 89% (89 mg); mp 153−155 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.38 (s,

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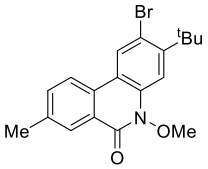
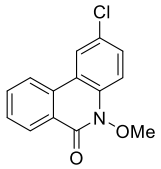
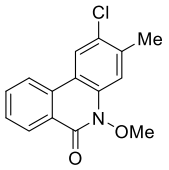
1H), 8.32 (s, 1H), 8.05 (d, J = 8.4 Hz, 1H), 7.72 (s, 1H), 7.58 (d, J = 8.4 Hz, 1H), 4.13 (s, 3H), 2.52 (s, 3H), 1.60 (s, 9H); $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 157.5, 149.5, 138.9, 134.3, 134.3, 130.1, 129.2, 128.5, 126.4, 121.9, 118.1, 116.7, 112.1, 62.8, 37.3, 29.8, 21.5; IR (KBr) $\tilde{\nu}$ = 2956, 2920, 2851, 1667, 1614, 1465, 1398, 1383, 1288, 1259, 1046, 1025, 876 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{19}H_{20}{}^{79}BrNO_2$ $[M + H]^+$ 374.0750, found 374.0750, $C_{19}H_{20}{}^{81}BrNO_2$ $[M + H]^+$ 376.0731, found 376.0732.



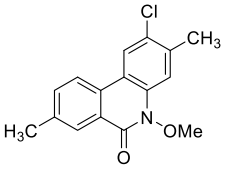
2-Chloro-5-methoxyphenanthridin-6(5H)-one (**4a**):[51] R_f = 0.55 (hexane/ethyl acetate 4:1); white solid; yield 94% (70 mg); ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.46 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 7.2 Hz, 2H), 7.74 (t, J = 7.6 Hz, 1H), 7.63−7.51 (m, 2H), 7.51−7.43 (m, 1H), 4.05 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 156.9, 134.3, 132.9, 131.8, 129.9, 128.9, 128.7, 128.5, 126.5, 123.0, 122.1, 119.8, 114.1, 62.8; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{11}ClNO_2$ $[M + H]^+$ 260.0473, found 260.0468.



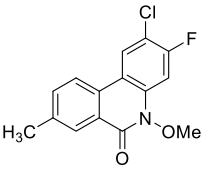
2-Chloro-5-methoxy-3-methylphenanthridin-6(5H)-one (**4b**):[57] R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 91% (103 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 8.0 Hz, 1H), 8.21 (s, 1H), 8.17 (d, J = 8.0 Hz, 1H), 7.78 (t, J = 7.2 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.54 (s, 1H), 4.14 (s, 3H), 2.55 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 156.9, 138.2, 134.2, 132.8, 131.9, 129.4, 128.4, 128.2, 126.1, 123.4, 121.8, 117.7, 114.5, 62.7, 20.6; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{13}ClNO_2$ $[M + H]^+$ 274.0629, found 274.0644.



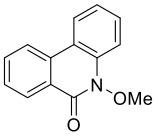
2-Chloro-5-methoxy-3,8-dimethylphenanthridin-6(5H)-one (**4i**): R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 87% (98 mg); mp 268−270 °C; ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.08 (s, 1H), 7.95 (s, 1H), 7.90−7.78 (m, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.31 (s, 1H), 3.92 (s, 3H), 2.33 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 156.7, 138.2, 137.3, 133.8, 133.5, 129.1, 128.9, 127.8, 125.6, 122.8, 121.6, 117.5, 114.1, 62.4, 21.0, 20.3; IR (KBr) $\tilde{\nu}$ = 3080, 2950, 2922, 1627, 1607, 1577, 1472, 1401, 1379, 1349, 1257, 1062, 1036, 939, 810 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{14}ClNaNO_2$ $[M + Na]^+$ 310.0605, found 310.0600.



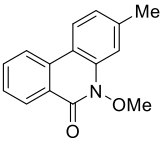
2-Chloro-3-fluoro-5-methoxy-8-methylphenanthridin-6(5H)-one (**4j**): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 85% (76 mg); mp 187−188 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.18 (d, J = 7.2 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 10.0 Hz, 1H), 4.12 (s, 3H), 2.51 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 158.6 (d, J = 250.7 Hz), 157.3, 139.1, 135.5 (d, J = 9.7 Hz), 134.5, 129.1, 128.6, 125.9, 125.2, 121.9, 116.2 (d, J = 19.0 Hz), 115.9 (d, J = 3.2 Hz), 101.2 (d, J = 27.4 Hz), 63.1, 21.5; IR (KBr) $\tilde{\nu}$ = 2951, 2921, 2852, 1663, 1617, 1588, 1480, 1427, 1326, 1281, 1241, 1186, 840 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{12}ClFNO_2$ $[M + H]^+$ 292.0535, found 292.0539.



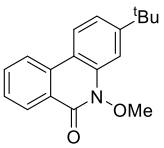
5-Methoxyphenanthridin-6(5H)-one (**2a**):[58] R_f = 0.55 (hexane/ethyl acetate 4:1); white solid; yield 97% (57.5 mg); ^1H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.21 (d, J = 8.0 Hz, 1H), 7.97 (dd, J = 7.6, 5.2 Hz, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.32−7.24 (m, 2H), 7.10−7.00 (m, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 157.2, 135.6, 132.9, 132.6, 129.9, 128.3, 128.0, 126.1, 123.2, 123.2, 121.9, 118.4, 112.5, 62.6; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{12}NO_2$ $[M + H]^+$ 226.0863, found 226.0865.



5-Methoxy-3-methylphenanthridin-6(5H)-one (**2b**):[53] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 94% (93 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 8.0 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.6 Hz, 1H), 7.47 (s, 1H), 7.15 (d, J = 8.0 Hz, 1H), 4.13 (s, 3H), 2.52 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.5, 140.7, 135.9, 133.2, 132.7, 128.6, 127.7, 126.0, 124.5, 123.2, 121.8, 116.8, 112.8, 62.8, 22.0, HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{13}NaNO_2$ $[M + Na]^+$ 262.0838, found 262.0825.



3-tert-Butyl-5-methoxyphenanthridin-6(5H)-one (**2d**): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 87% (88 mg); mp 122−124 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 8.0 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.4 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.68 (s, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 4.15 (s, 3H), 1.43 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.7, 153.9, 135.8, 133.2, 132.7, 128.7, 127.8, 126.2, 123.2, 121.9, 120.9, 116.3, 109.3, 62.7, 35.4, 31.4; IR (KBr) $\tilde{\nu}$ = 2962, 2919, 2851, 1659, 1606, 1574, 1475, 1413, 1320, 1250, 1175, 1045, 1004, 908, 807 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{18}H_{20}NO_2$ $[M + H]^+$ 282.1489, found 282.1512.



3-Fluoro-5-methoxyphenanthridin-6(5H)-one (**2e**):[58] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 92% (73 mg); ^1H NMR (400 MHz, $CDCl_3$) δ 8.52 (dd, J = 8.0, 1.2 Hz, 1H), 8.25−8.20 (m, 1H), 8.20−8.15 (m, 1H), 7.80−7.74 (m, 1H), 7.58 (dd, J = 11.2, 4.0 Hz, 1H), 7.36 (dd, J = 10.2, 2.8 Hz, 1H), 7.09−7.02 (m, 1H), 4.14 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J = 249.0 Hz), 157.6, 137.5 (d, J = 11.0 Hz), 133.0, 132.7, 128.8, 128.0, 125.8, 125.5 (d, J = 9.8 Hz), 121.9, 115.0 (d, J = 2.7 Hz), 111.1 (d, J = 22.8 Hz), 99.9 (d, J = 27.9 Hz), 63.0; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{11}FNO_2$ $[M + H]^+$ 244.0768, found 244.0771.

https://doi.org/10.1021/acs.joc.1c01742
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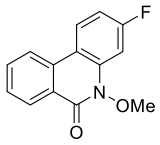
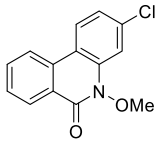
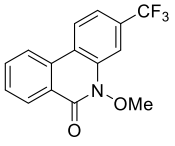


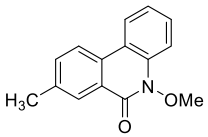
3-Chloro-5-methoxyphenanthridin-6(5H)-one (**2f**):[53] R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 89% (71 mg); ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.63 (dd, J = 8.0, 1.2 Hz, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 7.93−7.87 (m, 1H), 7.77 (d, J = 2.0 Hz. 1H), 7.75−7.69 (m, 1H), 7.44−7.39 (m, 1H), 4.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 157.3, 136.7, 136.1, 132.9, 132.3, 128.6, 128.4, 126.1, 124.6, 123.5, 122.0, 117.1, 112.6, 62.9; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{11}ClNO_2$ $[M + H]^+$ 260.0473, found 260.0474.



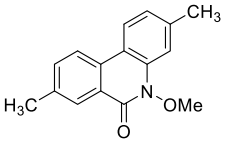
5-Methoxy-3-(trifluoromethyl)phenanthridin-6(5H)-one (**2g**):[58] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 93% (55.5 mg); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.59 (dd, J = 8.4, 0.7 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.31 (d, J = 8.4 Hz, 1H), 7.93 (s, 1H), 7.87−7.82 (m, 1H), 7.69 (dd, J = 11.2, 3.5 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 4.18 (s, 3H); ^{13}C{^{1}H} NMR (175 MHz, $CDCl_3$) δ 157.3, 136.1, 133.2, 131.9, 131.9 (q, J = 33.0 Hz), 129.4, 128.9, 127.1, 124.2, 123.9 (q, J = 272.5 Hz), 122.6, 121.4, 119.8 (q, J = 3.3 Hz), 63.2; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{11}F_3NO_2$ $[M + H]^+$ 294.0736, found 294.0727.



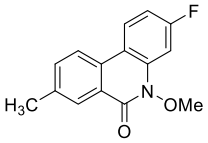
5-Methoxy-8-methylphenanthridin-6(5H)-one (**2h**):[58] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 88% (87 mg); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.47 (d, J = 8.0 Hz, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.16 (s, 1H), 7.69 (dd, J = 8.4, 1.6 Hz, 1H), 7.64 (d, J = 4.0 Hz, 2H), 7.42−7.30 (m, 1H), 4.02 (s, 3H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 156.1, 138.2, 135.1, 134.2, 130.2, 129.9, 127.3, 125.6, 123.6, 123.3, 122.8, 117.9, 112.2, 62.5, 20.9; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{14}NO_2$ $[M + H]^+$ 240.1019, found 240.1028.



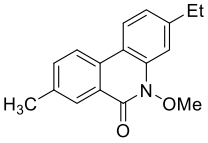
5-Methoxy-3,8-dimethylphenanthridin-6(5H)-one (**2i**):[53] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 89% (88 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.09 (dd, J = 8.0, 5.2 Hz, 2H), 7.56 (d, J = 8.0 Hz, 1H), 7.45 (s, 1H), 7.15 (d, J = 8.0 Hz, 1H), 4.14 (s, 3H), 2.51 (s, 3H), 2.49 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.7, 140.1, 137.9, 135.4, 134.1, 130.8, 128.3, 1258, 124.5, 123.0, 121.8, 116.4, 112.8, 62.8, 21.9, 21.4; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{15}NaNO_2$ $[M + Na]^+$ 276.0995, found 276.1008.



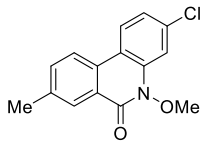
3-Fluoro-5-methoxy-8-methylphenanthridin-6(5H)-one (**2j**): R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 84% (67 mg); mp 190−192 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (dd, J = 8.4, 6.0 Hz, 1H), 8.34 (d, J = 8.4 Hz, 1H), 8.10 (s, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.42 (dd, J = 10.2, 1.6 Hz, 1H), 7.21 (dd, J = 12.0, 5.2 Hz, 1H), 4.03 (s, 3H), 2.46 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 163.4 (d, J = 245.6 Hz), 156.8, 138.5, 137.1 (d, J = 11.0 Hz), 134.8, 130.2, 127.8, 126.7 (d, J = 9.3 Hz), 125.4, 123.3, 115.1, 111.1 (d, J = 22.3 Hz), 99.8 (d, J = 27.9 Hz), 63.2, 21.3; IR (KBr) $\tilde{\nu}$ = 2954, 2916, 2848, 1660, 1617, 1593, 1482, 1426, 1328, 1266, 1171, 1037, 1010, 941, 836 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{13}FNO_2$ $[M + H]^+$ 258.0925, found 258.0936.



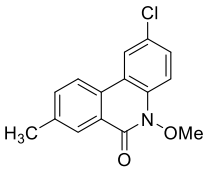
3-Ethyl-5-methoxy-8-methylphenanthridin-6(5H)-one (**2k**): R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 86% (68 mg); mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.13 (d, J = 3.6 Hz, 1H), 8.11 (d, J = 3.6 Hz, 1H), 7.56 (dd, J = 8.4, 1.6 Hz, 1H), 7.48 (s, 1H), 7.18 (dd, J = 8.4, 1.2 Hz, 1H), 4.13 (d, J = 4.4 Hz, 3H), 2.81 (q, J = 7.6 Hz, 2H), 2.51 (s, 3H), 1.33 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.7, 146.5, 137.9, 135.6, 134.0, 130.8, 128.3, 125.9, 123.3, 123.1, 121.9, 116.7, 111.7, 62.7, 29.3, 21.4, 15.7; IR (KBr) $\tilde{\nu}$ = 2922, 2852, 1707, 1646, 1613, 1482, 1458, 1327, 1284, 1159, 1097, 1065, 984, 862 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{17}H_{18}NO_2$ $[M + H]^+$ 268.1332, found 268.1334.



3-Chloro-5-methoxy-8-methylphenanthridin-6(5H)-one (**2l**): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 83% (66 mg); mp 191−193 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.17 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.98 (d, J = 8.4 Hz, 1H), 7.51 (d, J = 2.0 Hz, 1H), 7.48 (d, J = 8.4 Hz, 1H), 7.17 (dt, J = 8.4, 2.0 Hz, 1H), 4.01 (s, 3H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 157.1, 138.6, 136.0, 135.2, 134.1, 129.6, 128.0, 125.6, 124.2, 123.3, 121.9, 116.9, 112.3, 62.7, 21.2; IR (KBr) $\tilde{\nu}$ = 2915, 2847, 1659, 1618, 1537, 1425, 1312, 1137, 1091, 1039, 827 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{13}ClNO_2$ $[M + H]^+$ 274.0629, found 274.0629.



2-Chloro-5-methoxy-8-methylphenanthridin-6(5H)-one (**2m**): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 78% (62 mg); mp 182−184 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (s, 1H), 8.43 (d, J = 8.4 Hz, 1H), 8.13 (s, 1H), 7.67 (dd, J = 8.4, 1.6 Hz, 1H), 7.62 (s, 2H), 4.02 (s, 3H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 156.3, 139.4, 134.7, 134.4, 129.9, 129.6, 128.3, 127.8, 126.4, 123.7, 123.6, 120.1, 114.7, 63.2, 21.3; IR (KBr) $\tilde{\nu}$ = 2975, 2927, 1663, 1613, 1583, 1477, 1404, 1332, 1227, 1132, 1038, 848 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{15}H_{12}ClNaNO_2$ $[M + Na]^+$ 296.0449, found 296.0478.



5-Methoxy-2-nitrophenanthridin-6(5H)-one (**2o**): R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 88% (70 mg); mp 246−247 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.44 (d, J = 9.2 Hz, 1H), 8.37 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 9.2 Hz, 1H), 7.73 (d, J = 7.6 Hz, 1H), 4.18 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.3, 143.3, 140.1, 133.6, 131.8, 129.6, 128.9, 126.5, 124.9, 122.5, 119.6, 118.7, 113.4, 63.3; IR (KBr) $\tilde{\nu}$ = 3072, 2946, 1658, 1517, 1488, 1332, 1299, 1284, 1136, 1033,

https://doi.org/10.1021/acs.joc.1c01742
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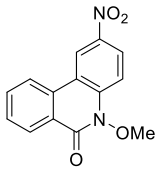
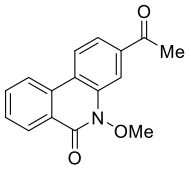
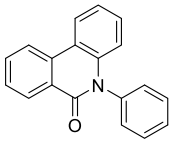
912 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{14}H_{11}N_2O_4$ $[M + H]^+$ 271.0713, found 271.0711.



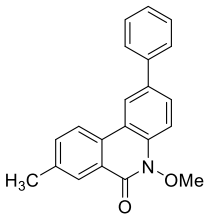
*Methyl 5-methoxy-6-oxo-5,6-dihydrophenanthridine-3-carboxylate (**2p**):* R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 91% (54 mg); mp 162−164 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (d, J = 8.0 Hz, 1H), 8.31 (dd, J = 11.2, 8.4 Hz, 2H), 8.20 (s, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.81 (t, J = 7.6 Hz, 1H), 7.66 (t, J = 7.6 Hz, 1H), 4.17 (s, 3H), 2.72 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.3, 157.3, 137.9, 136.0, 133.1, 132.1, 129.4, 128.8, 127.2, 123.8, 122.9, 122.8, 122.4, 112.7, 63.1, 27.1; IR (KBr) $\tilde{\nu}$ = 3071, 2939, 1680, 1657, 1605, 1509, 1412, 1316, 1278, 1246, 1175, 983 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{16}H_{14}NO_3$ $[M + H]^+$ 268.0968, found 268.0989.



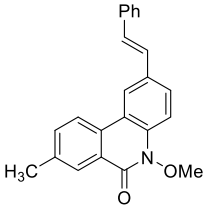
*5-Phenylphenanthridin-6(5H)-one (**2q**):*[67] R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 94% (37.4 mg); mp 220−222 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 8.0 Hz, 1H), 8.42−8.26 (m, 2H), 7.83 (t, J = 7.6 Hz, 1H), 7.63 (t, J = 7.6 Hz, 3H), 7.58−7.51 (m, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.33−7.28 (m, 2H), 6.76−6.66 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.9, 139.3, 138.4, 134.2, 133.0, 130.4, 129.3, 129.2, 129.2, 128.9, 128.3, 125.9, 123.1, 122.8, 121.9, 119.2, 117.2; IR (KBr) $\tilde{\nu}$ = 3056, 1651, 1602, 1502, 1484, 1332, 1317, 1174, 1160, 1075, 756 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{19}H_{14}NO$ $[M + H]^+$ 272.1070, found 272.1077.



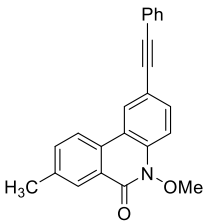
*5-Methoxy-8-methyl-2-phenylphenanthridin-6(5H)-one (**5**):* R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 95% (75 mg); mp 162−164 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.38 (s, 1H) 8.24 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 7.0 Hz, 2H), 7.61 (d, J = 7.7 Hz, 1H), 7.50 (t, J = 7.0 Hz, 2H), 7.40 (t, J = 7.0 Hz, 1H), 4.17 (s, 3H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 157.5, 140.5, 138.7, 136.6, 134.8, 134.2, 130.6, 129.1, 128., 128.5, 127.6, 127.3, 126.4, 122.1, 121.6, 119.2, 113.3, 62.9, 21.5; IR (KBr) $\tilde{\nu}$ = 3131, 2962, 2926, 2848, 1637, 1615, 1538, 1323, 1158, 1320, 1068, 1038, 1019, 947, 854 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{21}H_{18}NO_2$ $[M + H]^+$ 316.1332, found 316.1336.



*(E)-5-Methoxy-8-methyl-2-styrylphenanthridin-6(5H)-one (**6**):* R_f = 0.50 (hexane/ethyl acetate 4:1); white solid; yield 92% (59 mg); mp 132−134 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.30 (s, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 7.7 Hz, 2H), 7.39 (t, J = 7.7 Hz, 2H), 7.29 (t, J = 7.0 Hz, 1H), 7.20 (q, J = 16.1 Hz, 2H), 4.15 (s, 3H), 2.54 (s, 3H); $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 157.3, 138.7, 137.3, 134.9, 134.2, 132.7, 130.5, 128.9, 128.8, 128.5, 127.9, 127.8, 127.5, 126.6, 126.5, 122.1, 121.3, 119.0, 113.2, 62.9, 21.5; IR (KBr) $\tilde{\nu}$ = 3057, 3022, 2946, 2920, 2849, 1668, 1633, 1614, 1594, 1495, 1435, 1326, 1289, 1231, 1143, 1041, 963, 814 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{23}H_{20}NO_2$ $[M + H]^+$ 342.1489, found 342.1489.



*5-Methoxy-8-methyl-2-(phenylethynyl)phenanthridin-6(5H)-one (**7**).* R_f = 0.45 (hexane/ethyl acetate 4:1); white solid; yield 82% (52.5 mg); mp 180−182 °C; ^1H NMR (700 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.32 (d, J = 1.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 1H), 7.63 (dd, J = 8.4, 1.4 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.55 (s, 1H), 7.53 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 7.0 Hz, 1H), 7.29 (t, J = 7.0 Hz, 2H), 4.12 (s, 3H), 2.53 (s, 3H); $^{13}C\{^1H\}$ NMR (175 MHz, $CDCl_3$) δ 157.2, 139.4, 134.6, 134.4, 134.4, 134.3, 132.3, 131.7, 129.7, 129.4, 128.6, 128.5, 128.5, 126.6, 125.9, 122.2, 120.6, 116.4, 114.5, 62.9, 21.5; IR (KBr) $\tilde{\nu}$ = 3053, 2941, 2917, 2818, 1664, 1615, 1584, 1477, 1432, 1329, 1299, 1225, 1035, 959, 841 cm^{-1}; HR-MS (ESI-TOF) m/z calcd for $C_{23}H_{18}NO_2$ $[M + H]^+$ 340.1332, found 340.1333.



■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01742.

Experimental details, data and spectra (NMR, EPR, UV−vis, and fluorescence), X-ray crystallography details (PDF)

FAIR data, including the primary NMR FID files, for compounds **2a**, **2b**, **2d**−**2q**, **3a**−**3f**, **3h**−**3l**, **3n**, **4a**, **4b**, **4i**, **4j**, **5**−**7** (ZIP)

Accession Codes

CCDC 2074176−2074177 and 2074179 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

Experimental aspects were carried out by S.K.B. The manuscript was written through contributions of both authors.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

S.K.B. thanks the DST (INSPIRE) for fellowships. We also thank CSIR for funding Project No. 02(0338)/18/EMR-II (PM). We thank Dr. Md. Toufique Alam for his valuable suggestion and discussion.

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https://doi.org/10.1021/acs.joc.1c01742
J. Org. Chem. XXXX, XXX, XXX−XXX