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Kinetic Control of Rh(III)-Catalyzed Annulation of C−H Bonds with Quinones: Chemoselective Synthesis of Hydrophenanthridinones and Phenanthridinones

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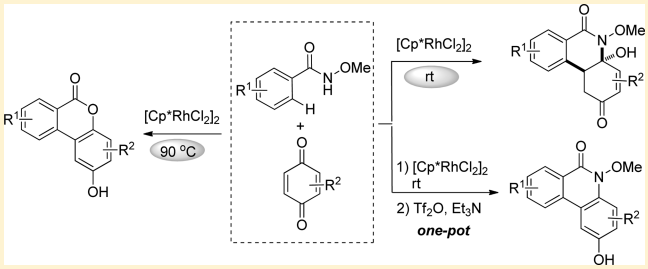
Supporting Information

ABSTRACT: A temperature-dependent redox-neutral Rh(III)-catalyzed C−H bond annulation of *N*-methoxybenzamides with quinones was developed for the chemoselective synthesis of hydrophenanthridinones and phenanthridinones. This reaction involves an Rh(III)-catalyzed C−H bond functionalization and a subsequent cyclization through the directing group nucleophilic addition to the carbonyl group at room temperature.



INTRODUCTION

The phenanthridine and hydrophenanthridine structural motifs are the core of many natural products with pharmacological relevance (Figure 1),[1−5] such as ethidium,[1b,2] trispheridine,[3]

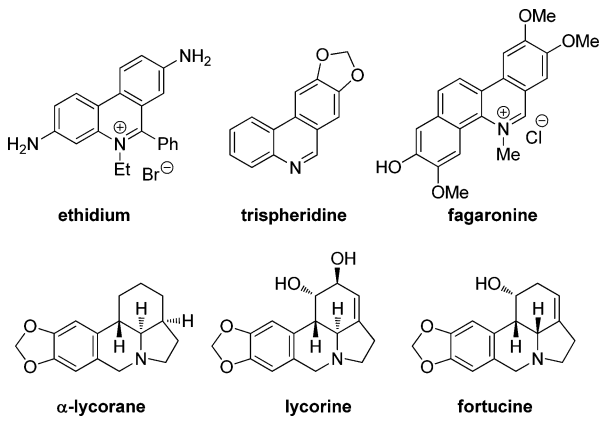


Figure 1. Representative natural products.

fagaronine,[4] and lycorane-type alkaloids (α-lycorane, lycorine, and fortucine).[5] Therefore, a number of synthetic methods for the construction of these frameworks have been reported.[1−6] Generally, these methods rely on the intramolecular C−N or C−C bond formation to construct the central pyridine ring under either radical cyclization conditions or transition metal catalysis by using 2-isocyanobiphenyls,[1a] biaryl-2-acyl oximes,[6b] or other biaryl compounds[6c] as the starting materials.

Rh(III)-catalyzed C−H functionalization has rapidly emerged as a versatile and straightforward synthetic protocol for the construction of heterocycles.[7] This strategy obviates prefunctionalization of the starting materials, thus dramatically improving the overall efficiency in an atom- and step-economical manner. To date, various heterocycles have been successfully constructed using this methodology.[7,8] Recently, Cheng and co-workers developed efficient Rh-catalyzed oxidative annulations of aryl C−H bonds with either aryl boronic acids[9] or aryltriethoxysilanes[10] to synthesize phenanthrines through a double C−H bond activation strategy; however, a large amount of oxidants (Ag^+ and/or Cu^{2+} salt) is necessary (Scheme 1, eq 1).

In 2015, we reported an Rh(III)-catalyzed oxidative C−H bond arylation with hydroquinones for the sustainable synthesis of dibenzo[*b*,*d*]pyran-6-ones and benzo[*d*]naphtho[1,2-*b*]-pyran-6-ones at elevated temperatures (Scheme 1, eq 2).[11] Mechanistic investigation indicated that the quinone could be produced under the standard conditions and could serve as the coupling partner in this Rh(III)-catalyzed reaction. Although benzoquinone is a cheap and commercially available chemical, few articles report on the C−H bond functionalization reaction using benzoquinone as a coupling partner.[12] Herein, we report an Rh(III)-catalyzed redox-neutral C−H bond annulation of *N*-methoxybenzamides with quinones at room temperature for divergent construction of tricyclic hydrophenanthridone scaffolds (Scheme 1, eq 3). This protocol enables the convenient assembly of phenanthridones by a one-pot sequential Rh(III)-catalyzed aryl C−H bond annulation and aromatization (Scheme 1, eq 4). Furthermore, it is worth mentioning that distinct types of complex molecules are constructed from identical starting materials using the same catalyst system by tuning the role of the directing group, which acts selectively as a nucleophile in these transformations

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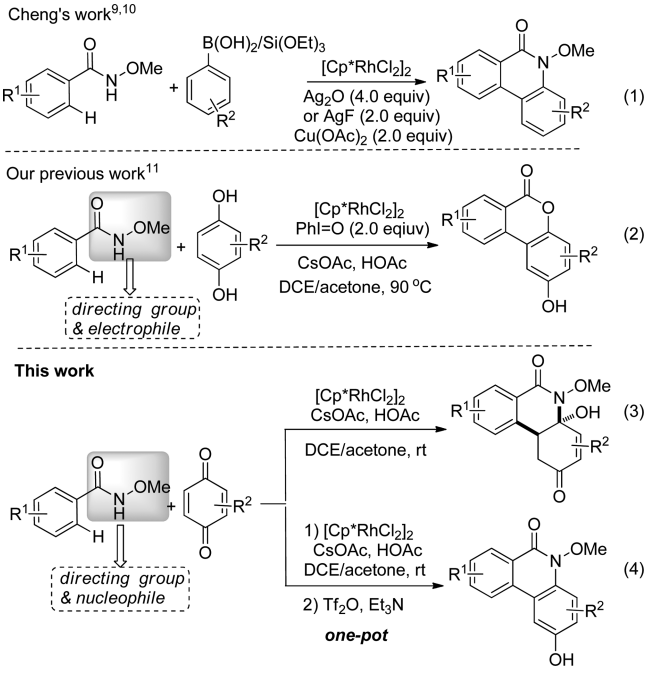
Scheme 1. Divergent Annulation of Aryl C−H Bonds with Quinones

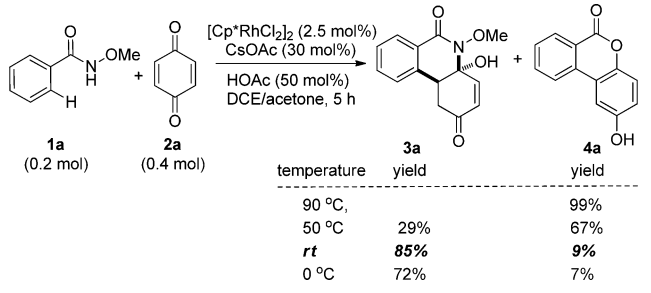


(Scheme 1, eqs 3 and 4). In our previous work, the directing group acted as an electrophile (Scheme 1, eq 2).[11]

RESULTS AND DISCUSSION

In this study, the reaction of amide **1a** with quinone **2a** was employed as model to optimize the reaction conditions (Scheme 2). It was found that hydrophenanthridone **3a**

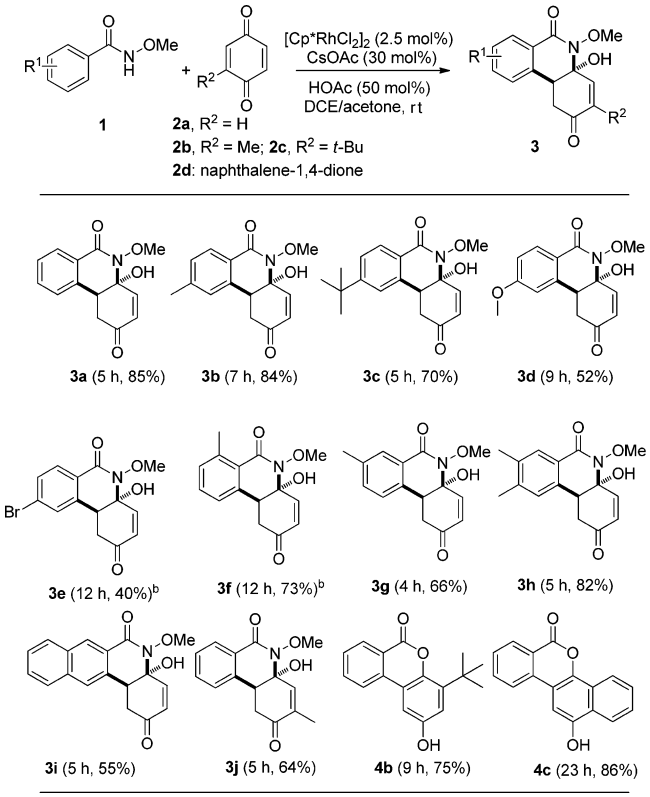
Scheme 2. Temperature-Dependent Annulation of Amide 1a with Quinone 2a



temperature	3a yield	4a yield
90 °C,		99%
50 °C	29%	67%
rt	***85%***	***9%***
0 °C	72%	7%

became the major product when amide **1a** and quinone **2a** were treated with the reported reaction conditions[11] ($(Cp^*RhCl_2)_2$ (2.5 mol %), CsOAc (30 mol %), and acetic acid (0.5 equiv)) upon decreasing the reaction temperature (Scheme 2). To our delight, hydrophenanthridone **3a** was chemo- and diastereoselectively obtained in 85% yield when the annulation of amide **1a** and quinone **2a** was performed at room temperature. It is very interesting that the chemoselectivity of this annulation was tuned by only a slight change of the reaction temperature. In this case, tricyclic hydrophenanthridone **3a** was the major product, whereas in our previous work,[11] dibenzo[*b*,*d*]pyran-6-one **4a** was the sole product. The scope of this divergent annulation of amides **1** with quinone **2** was explored, and the results are summarized in Table 1.

Table 1. Synthesis of Hydrophenanthridones 3[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), $(Cp^*RhCl_2)_2$ (2.5 mol %), CsOAc (30 mol %), HOAc (50 mol %), DCE/acetone (1 mL/1 mL). [b]5 mol % $(Cp^*RhCl_2)_2$ was used.

At room temperature, the reactions of various *N*-methoxybenzamides **1** with quinones **2** proceeded smoothly to afford a wide range of hydrophenanthridones **3** in a highly diastereoselective manner in good to high yields (Table 1). Amides **1** with both electron-donating (Table 1, **3b**−**d**) and electron-withdrawing (Table 1, **3e**) groups at the *para* position of aryl groups participated well in this reaction, and the corresponding products were obtained in good to high yields.[13] Benzamides **1** with ortho-, meta-, and disubstitution reacted smoothly to give the corresponding hydrophenanthridones (Table 1, **3f**−**h**) in high yields. In the case of *β*-naphthamide **1n**, tetrahydrobenzo[*j*]phenanthridine-2,6-dione **3i** was obtained in good yield. For the quinone derivatives, methyl quinone **2b** exclusively afforded the 3-methyl tetrahydrophenanthridine-2,6-dione **3j** in good yield (the configuration of **3j** was confirmed by HMBC; see Supporting Information), whereas the bulky *tert*-butyl quinone **2c** and naphthoquinone **2d** gave dibenzo[*b*,*d*]pyran-6-one **4b** and benzo[*d*]naphtho[1,2-*b*]pyran-6-one **4c**, respectively. It is important to note that the annulation is highly regioselective with respect to the unsymmetrical quinones **2b** and **2c** at room temperature.

Structurally, the hydrophenanthridones **3** containing a 4-hydroxycyclohex-2-enone moiety could aromatize after elimination of water and tautomerization. Thus, a one-pot synthesis of phenanthridonones **5** from the annulation of amides **1** and quinones **2** was accomplished by adding Tf_2O and triethyl amine to improve the elimination of the hydroxy group. As shown in Table 2, this one-pot protocol tolerates various aromatic amides **1** and provides the corresponding phenanthridines **5** in good to high yields. Although Rh(III)-catalyzed

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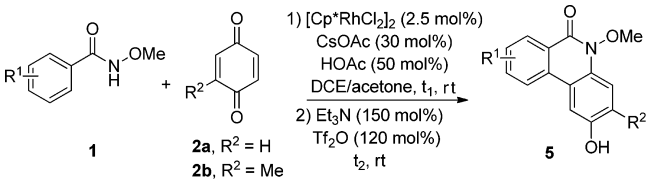
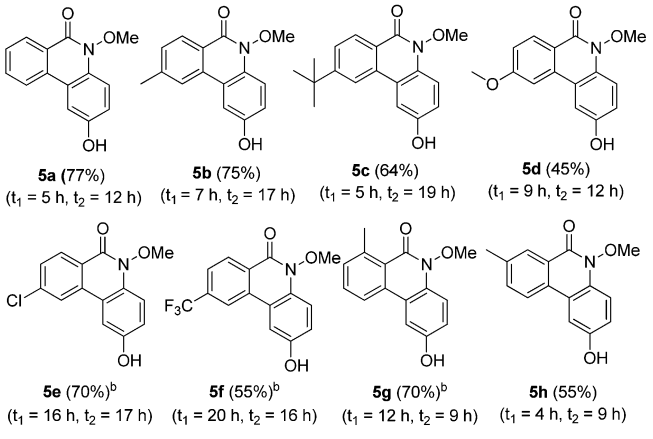
Table 2. Synthesis of Phenanthridones 5[a]





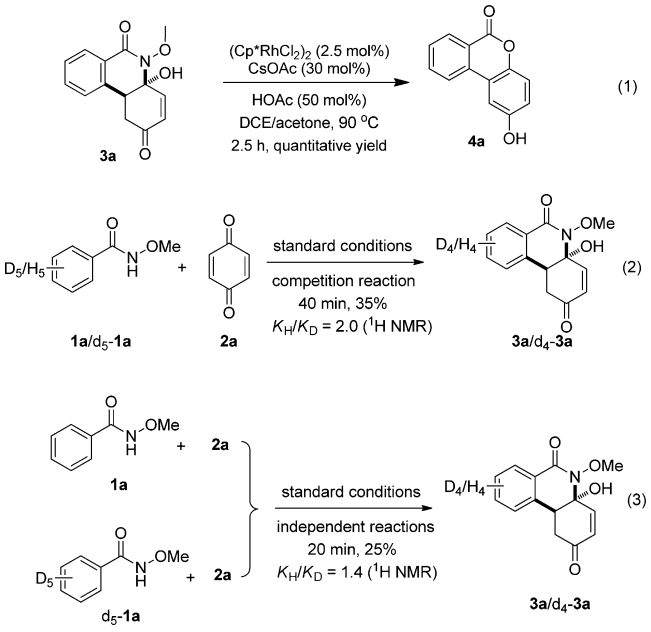
[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), $(Cp^*RhCl_2)_2$ (2.5 mol %), CsOAc (30 mol %), and HOAc (50 mol %) in DCE/acetone (1 mL/1 mL) for time 1; then Et_3N (150 mol %) and Tf_2O (120 mol %) for time 2. [b]5 mol % $(Cp^*RhCl_2)_2$ was used.

annulation of aryl C−H with preactivated coupling partners such as aryl boronic acids[9] and arylsilanes[10] has been reported, this one-pot protocol is still appealing due to its mild, redox-neutral reaction conditions and readily available starting materials.

To shed light on the reaction mechanism of this divergent annulation, hydrophenanthridone **3a** was treated with the standard conditions ($(Cp^*RhCl_2)_2$ (2.5 mol %), CsOAc (30 mol %), and acetic acid (0.5 equiv)) at 90 °C for 2.5 h, and dibenzo[*b*,*d*]pyran-6-one **4a** was obtained in quantitative yield (Scheme 3, eq 1). This result confirms that the hydrophenanthridone **3a** is the product of kinetic control which is easily converted to the stable **4a** of thermodynamic control at a higher temperature. Next, a deuterium-labeling experiment was carried out, which showed competition between protio and deutero **1a** with a 2:1 product ratio at early conversion (Scheme 3, eq 2). In addition, the kinetic isotope effect (KIE) was further measured from two side-by-side reactions using protio and deutero **1a** (Scheme 3, eq 3), and a KIE value of 1.4 was observed. These results demonstrate that the C−H bond cleavage process may not be involved in the rate-determining step.

On the basis of our previous observations,[11] present observations, and literature precedent,[12,14−17] a mechanistic pathway is proposed (Scheme 4, taking the reaction of amide **1a** with quinone **2a** as an example). First, C−H bond cleavage

Scheme 3. Control Experiments



of **1a** occurs to produce a five-membered rhodacycle intermediate **A**. Next, coordination of the benzoquinone affords intermediate **B**, which undergoes migratory insertion into the incipient Rh−C bond to form a seven-membered rhodacycle **C**.[14,15] Protonolysis delivers intermediate **D** while concomitantly releasing the catalyst Cp^*RhX_2. Then, the cyclohexendione intermediate **D** proceeds via the two competing pathways depicted as follows. In path a, for the formation of dibenzo[*b*,*d*]pyran-6-one **4a**, tautomerization of **D** generates diphenol intermediate **E**, which is followed by nucleophilic substitution to furnish the product **4a** with the release of an *O*-methylhydroxamine under metal- or acid-catalyzed conditions.[16] In path b, for the formation of hydrophenanthridinone **3a** and phenanthridinone **5a**, a reversible intramolecular nucleophilic addition of intermediate **D** forms hydrophenanthridinone **3a**, which produces compound **5a** by a one-pot tandem triflation, elimination, and aromatization sequence. The proposed mechanism in Scheme 4 suggests that the amide group of substrate **1** is a multitasking functional directing group which acts as both a directing group and an electrophile in path a and both a directing group and a nucleophile in path b.

In summary, a novel, temperature-dependent Rh(III)-catalyzed C−H bond annulation with readily available, inexpensive quinones was developed for the divergent and convenient synthesis of hydrophenanthridinones and phenanthridinones. In these transformations, the bifunctional directing groups were incorporated into the products while serving selectively as nucleophiles in the final cyclization step. The reaction features high efficiency, atom- and step-economy, broad substrate scope, good functional group tolerance, and good chemo- and diastereoselectivity. Kinetic control of the annulation of aryl C−H bonds with quinones, complementing that of our previous thermodynamic control,[11] represents an efficient protocol for the divergent synthesis of complex natural product scaffolds from identical, readily available starting materials.

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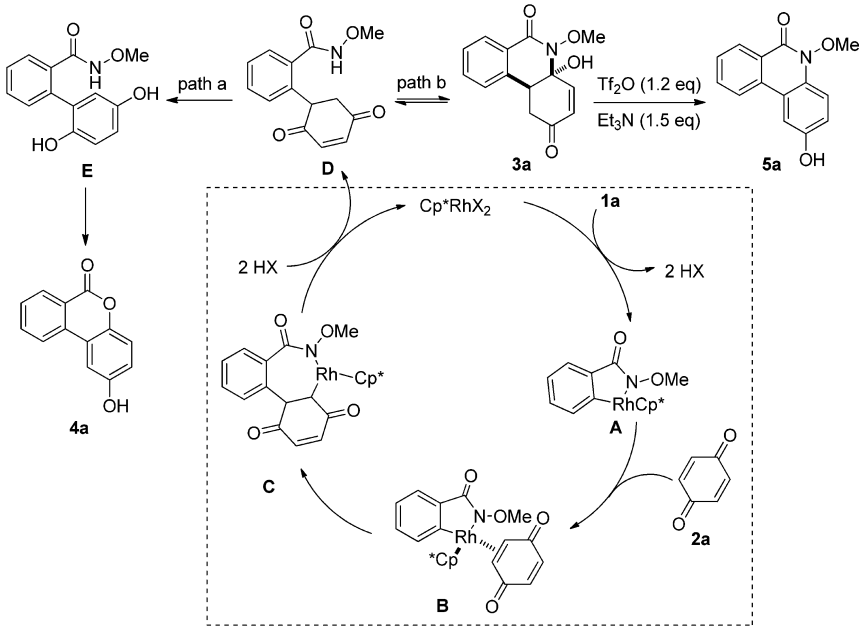
Scheme 4. Proposed Mechanism



EXPERIMENTAL SECTION

General Procedures for Compounds 3a–j (with the Reaction of 1a as an Example). Without any particular precautions to extrude oxygen or moisture, to a stirred mixture of **1a** (30.2 mg, 0.2 mmol) and **2a** (43.2 mg, 0.4 mmol) in DCE/acetone (1.0 mL/1.0 mL) were added $(Cp^*RhCl_2)_2$ (3.1 mg, 0.005 mmol), CsOAc (11.5 mg, 0.06 mmol), and HOAc (6.0 μL, 0.1 mmol), successively. The reaction mixture was stirred at room temperature for 5 h, and then **1a** was consumed as indicated by TLC. The reaction mixture was diluted with brine (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organics were dried (Na_2SO_4) and concentrated *in vacuo* at 35 °C. The residue was purified by column chromatography (petroleum ether/EtOAc = 7/1, v/v) to afford the desired product **3a** (85% yield).

General Procedures for the Synthesis of 5a–k (with the Reaction of 1a as an Example). According to the general procedure to afford **3a**, when the substrate **1a** was consumed (detected by TLC), Et_3N (0.3 mmol, 42.0 μL) and Tf_2O (0.24 mmol, 40.0 μL) were added to the reaction mixture directly. The resulting mixture was stirred at room temperature until **3a** was consumed as indicated by TLC. The reaction mixture was diluted with brine (10 mL) and extracted with EtOAc (2 × 10 mL). The combined organics were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (petroleum ether/EtOAc = 5/1, v/v) to afford the desired product **5a** (77% yield).

*4a-Hydroxy-5-methoxy-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3a**).* Yellowish solid (44.0 mg, 85%). Mp 205–206 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.54–2.67 (m, 2H), 3.72–3.74 (m, 4H), 6.16 (d, *J* = 10.5 Hz, 1H), 7.04 (d, *J* = 10.0 Hz, 1H), 7.29 (s, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.96 (d, *J* = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 43.4, 46.4, 63.9, 85.7, 126.7, 127.8, 127.9, 128.5, 128.7, 133.7, 139.3, 147.9, 163.4, 197.0. HRMS (ESI-TOF) *m/z*: calcd for $C_{14}H_{13}NNaO_4^+$ [Na + H]$^+$ 282.0737; found 282.0745.

*4a-Hydroxy-5-methoxy-9-methyl-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3b**).* Yellowish solid (45.9 mg, 84%). Mp 201–202 °C. ^{1}H NMR (400 MHz, DMSO): δ 2.65 (s, 3H), 2.70–2.75 (m, 2H), 3.79 (dd, *J* = 5.2, 12.4 Hz, 1H), 3.85 (s, 3H), 6.29 (d, *J* = 10.0 Hz, 1H), 7.17 (d, *J* = 10.0 Hz, 1H), 7.38–7.40 (m, 3H), 7.99 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 21.7, 43.4, 46.4, 63.9, 85.8, 124.2, 128.0, 128.6, 128.7, 128.9, 139.3, 144.0, 148.0, 163.5, 197.1. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{16}NO_4^+$ [M + H]$^+$ 274.1074; found 274.1079.

*9-tert-Butyl-4a-hydroxy-5-methoxy-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3c**).* Yellowish solid (44.1 mg, 70%). Mp 206–207 °C. ^{1}H NMR (500 MHz, DMSO): δ 1.30 (s, 9H), 2.56–2.65 (m, 2H), 3.71–3.75 (m, 4H), 6.15 (d, *J* = 10.0 Hz, 1H), 7.03 (d, *J* = 10.0 Hz, 1H), 7.26 (s, 1H), 7.47 (s, 2H), 7.88 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 31.3, 35.4, 43.6, 46.6, 63.9, 85.8, 124.2, 124.9, 125.4, 127.8, 128.7, 139.1, 148.1, 156.8, 163.5, 197.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{22}NO_4^+$ [M + H]$^+$ 316.1543; found 316.1548.

*4a-Hydroxy-5,9-dimethoxy-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3d**).* Yellowish solid (30.0 mg, 52%). Mp 173–174 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.60 (d, *J* = 9.0 Hz, 2H), 3.65 (t, *J* = 9.0 Hz, 1H), 3.70 (s, 3H), 3.82 (s, 3H), 6.14 (d, *J* = 10.5 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 1H), 7.01–7.04 (m, 2H), 7.22 (s, 1H), 7.88 (d, *J* = 9.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 43.3, 46.6, 56.1, 63.9, 85.8, 113.1, 114.0, 119.4, 128.6, 130.1, 141.6, 148.2, 163.5, 163.5, 197.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{15}NNaO_5^+$ [M + Na]$^+$ 312.0842; found 312.0850.

*9-Bromo-4a-hydroxy-5-methoxy-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3e**).* Yellowish solid (27.0 mg, 40%). Mp 223–224 °C. ^{1}H NMR (400 MHz, DMSO): δ 2.58–2.68 (m, 2H), 3.71–3.75 (m, 4H), 6.17 (d, *J* = 10.0 Hz, 1H), 7.03 (d, *J* = 10.0 Hz, 1H), 7.38 (s, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.75 (s, 1H), 7.87 (d, *J* = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 44.0, 46.7, 64.0, 85.9, 125.1, 127.8, 129.4, 129.8, 131.9, 135.1, 135.5, 148.1, 163.2, 197.1. HRMS (ESI-TOF) *m/z*: calcd for $C_{14}H_{13}BrNO_4^+$ [M + H]$^+$ 338.0022; found 338.0027.

*4a-Hydroxy-5-methoxy-7-methyl-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3f**).* Yellowish solid (39.9 mg, 73%). Mp 140–141 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.53–2.61 (m, 2H), 2.65 (s, 3H), 3.66 (dd, *J* = 4.5, 13.0 Hz, 1H), 3.70 (s, 3H), 6.14 (d, *J* = 10.0 Hz, 1H), 7.02 (d, *J* = 10.0 Hz, 1H), 7.16 (s, 1H), 7.24 (q, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 23.3, 43.8, 46.8, 63.7, 85.0, 124.3, 127.0, 128.6, 131.7, 132.8, 140.6, 141.3, 148.3, 164.2, 197.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{15}NNaO_4^+$ [M + Na]$^+$ 296.0893; found 296.0897.

*4a-Hydroxy-5-methoxy-8-methyl-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3g**).* Yellowish solid (36.0 mg, 66%). Mp 183–184 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.35 (s, 3H), 2.54–2.63 (m, 2H), 3.67 (d, *J* = 12.0 Hz, 1H), 3.71 (s, 3H), 6.14 (d, *J* = 10.0 Hz, 1H), 7.02 (d, *J* = 10.0 Hz, 1H), 7.25 (s, 1H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.40 (d, *J* = 7.0 Hz, 1H), 7.77 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 21.1, 43.4, 46.0, 63.9, 85.8, 126.5, 128.1, 128.5, 128.7, 134.4, 136.4, 137.3,

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148.0, 163.5, 197.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{15}NNaO_4^+$ $[M + Na]^+$ 296.0893; found 296.0879.

4a-Hydroxy-5-methoxy-8,9-dimethyl-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3h**). Yellowish solid (47.1 mg, 82%). Mp 197−198 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.26 (s, 6H), 2.55−2.58 (m, 2H), 3.60 (dd, J = 4.5, 12.0 Hz, 1H), 3.70 (s, 3H), 6.13 (d, J = 10.0 Hz, 1H), 7.01 (d, J = 10.5 Hz, 1H), 7.18 (d, J = 7.0 Hz, 2H), 7.71 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 19.5, 20.1, 43.4, 46.0, 63.9, 85.9, 124.3, 128.6, 128.7, 129.4, 136.1, 136.8, 142.8, 148.0, 163.7, 197.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{17}NNaO_4^+$ $[M + Na]^+$ 310.1050; found 310.1047.

4a-Hydroxy-5-methoxy-1,4a,5,12b-tetrahydrobenzo[j]-phenanthridine-2,6-dione (**3i**). Yellowish solid (34.0 mg, 55%). Mp 216−217 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.62 (d, J = 14.0 Hz, 1H), 2.77 (t, J = 14.0 Hz, 1H), 3.77 (s, 3H), 3.90 (d, J = 10.5 Hz, 1H), 6.19 (d, J = 10.0 Hz, 1H), 7.08 (d, J = 9.5 Hz, 1H), 7.37 (s, 1H), 7.58 (s, 1H), 7.65 (s, 1H), 7.93 (s, 2H), 8.14 (d, J = 7.5 Hz, 1H), 8.64 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 44.0, 46.7, 64.0, 85.9, 125.1, 127.1, 127.2, 127.8, 129.0, 129.1, 129.4, 129.8, 131.9, 135.1, 135.5, 148.1, 163.2, 197.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{15}NNaO_4^+$ $[M + Na]^+$ 332.0893; found 332.0897.

4a-Hydroxy-5-methoxy-3-methyl-1,4a,5,10b-tetrahydrophenanthridine-2,6-dione (**3j**). Yellowish solid (34.9 mg, 64%). Mp 182−183 °C. ^{1}H NMR (400 MHz, DMSO): δ 1.81 (s, 3H), 2.59−2.64 (m, 2H), 3.69−3.72 (m, 4H), 6.82 (d, J = 1.2 Hz, 1H), 7.14 (s, 1H), 7.41−7.45 (m, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.95 (d, J = 7.6 Hz, 1H). ^{13}C NMR (125 MHz, DMSO): δ 15.5, 43.4, 46.0, 63.8, 86.2, 126.8, 127.7, 127.8, 128.5, 133.6, 135.0, 139.2, 143.0, 163.2, 197.0. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{15}NNaO_4^+$ $[M + Na]^+$ 296.0893; found 296.0884.

The spectra of compounds **4b** and **4c** are consistent with our previous work[11] and ^{1}H NMR (see Supporting Information).

2-Hydroxy-5-methoxyphenanthridin-6(5H)-one (**5a**). Yellowish solid (37.1 mg, 77%). Mp 215−216 °C. ^{1}H NMR (500 MHz, DMSO): δ 4.00 (s, 3H), 7.14 (d, J = 9.0 Hz, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.66 (t, J = 7.0 Hz, 1H), 7.79 (s, 1H), 7.85 (t, J = 7.0 Hz, 1H), 8.34−8.38 (m, 2H), 9.72 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 62.9, 109.2, 114.3, 119.1, 119.5, 123.2, 126.5, 128.2, 128.8, 129.0, 132.8, 133.3, 154.1, 155.9. HRMS (ESI-TOF) *m/z*: calcd for $C_{14}H_{12}NO_3^+$ $[M + H]^+$ 242.0812; found 242.0816.

2-Hydroxy-5-methoxy-9-methylphenanthridin-6(5H)-one (**5b**). Yellowish solid (38.3 mg, 75%). Mp 208−209 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.5 (s, 3H), 3.97 (s, 3H), 7.11 (d, J = 7.5 Hz, 1H), 7.45 (s, 2H), 7.77 (s, 1H), 8.16 (s, 1H), 8.20 (d, J = 7.5 Hz, 1H), 9.65 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 22.0, 62.9, 109.2, 114.2, 119.0, 119.5, 123.1, 124.2, 128.2, 129.1, 130.0, 132.8, 143.6, 154.0, 155.9. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{14}NO_3^+$ $[M + H]^+$ 256.0968; found 256.0971.

9-tert-Butyl-2-hydroxy-5-methoxyphenanthridin-6(5H)-one (**5c**). Yellowish solid (38.0 mg, 64%). Mp 199−200 °C. ^{1}H NMR (500 MHz, DMSO): δ 1.41 (s, 9H), 3.99 (s, 3H), 7.13 (dd, J = 2.0, 9.0 Hz, 1H), 7.49 (d, J = 9.0 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 2.0 Hz, 1H), 8.27−8.28 (m, 2H), 9.65 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 31.4, 35.8, 62.9, 109.2, 114.2, 118.9, 119.1, 119.7, 124.3, 126.6, 128.2, 129.1, 132.5, 154.0, 155.7, 156.3. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{20}NO_3^+$ $[M + H]^+$ 298.1438; found 298.1427.

2-Hydroxy-5,9-dimethoxyphenanthridin-6(5H)-one (**5d**). Yellowish solid (24.4 mg, 45%). Mp 195−196 °C. ^{1}H NMR (500 MHz, DMSO): δ 3.97 (s, 3H), 3.98 (s, 3H), 7.14 (dd, J = 2.5, 9.0 Hz, 1H), 7.22 (dd, J = 2.0, 8.5 Hz, 1H), 7.47 (d, J = 9.0 Hz, 1H), 7.74 (d, J = 2.0 Hz, 1H), 7.83 (d, J = 2.5 Hz, 1H), 8.25 (d, J = 8.5 Hz, 1H), 9.66 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 56.3, 62.9, 105.6, 109.7, 114.1, 117.2, 119.3, 119.3, 119.9, 129.3, 130.3, 134.9, 153.9, 155.7, 163.3. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{14}NO_4^+$ $[M + H]^+$ 272.0917; found 272.0912.

9-Chloro-2-hydroxy-5-methoxyphenanthridin-6(5H)-one (**5e**). Yellowish solid (38.5 mg, 70%). Mp 236−237 °C. ^{1}H NMR (500 MHz, DMSO): δ 4.00 (s, 3H), 7.18 (d, J = 9.0 Hz, 1H), 7.51 (d, J = 9.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.84 (s, 1H), 8.32 (d, J = 8.5 Hz, 1H), 8.48 (s, 1H), 9.74 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 63.0, 109.8, 114.4, 118.6, 119.9, 123.0, 125.2, 128.9, 129.4, 130.4, 134.6, 138.7, 154.2, 155.3. HRMS (ESI-TOF) *m/z*: calcd for $C_{14}H_{11}ClNO_3^+$ $[M + H]^+$ 276.0422; found 276.0420.

9-(Trifluoromethyl)-2-hydroxy-5-methoxyphenanthridin-6(5H)-one (**5f**). Yellowish solid (34.0 mg, 55%). Mp 234−235 °C. ^{1}H NMR (500 MHz, DMSO): δ 4.02 (s, 3H), 7.21 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 9.0 Hz, 1H), 7.97 (s, 2H), 8.53 (d, J = 8.5 Hz, 1H), 8.72 (s, 1H), 9.76 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 63.1, 109.8, 114.4, 118.8, 120.1, 120.7, 124.3 (q, J = 271.6 Hz), 124.6, 129.3, 129.7, 133.1 (q, J = 31.9 Hz), 133.4, 154.4, 155.0. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{11}F_3NO_3^+$ $[M + H]^+$ 310.0686; found 310.0689.

2-Hydroxy-5-methoxy-7-methylphenanthridin-6(5H)-one (**5g**). Yellowish solid (35.7 mg, 70%). Mp 199−200 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.86 (s, 3H), 3.96 (s, 3H), 7.11 (d, J = 7.5 Hz, 1H), 7.42 (s, 2H), 7.68 (s, 1H), 7.75 (s, 1H), 8.22 (d, J = 7.5 Hz, 1H), 9.63 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 24.3, 62.6, 109.4, 113.8, 119.1, 119.4, 121.4, 124.6, 129.2, 132.2, 132.5, 134.2, 142.0, 153.8, 156.9. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{13}NNaO_3^+$ $[M + Na]^+$ 278.0788; found 278.0791.

2-Hydroxy-5-methoxy-8-methylphenanthridin-6(5H)-one (**5h**). Yellowish solid (28.1 mg, 55%). Mp 214−215 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.48 (s, 3H), 3.99 (s, 3H), 7.11 (d, J = 9.0 Hz, 1H), 7.48 (d, J = 9.0 Hz, 1H), 7.67 (d, J = 8.5 Hz, 1H), 7.75 (s, 1H), 8.15 (s, 1H), 8.27 (d, J = 8.0 Hz, 1H), 9.68 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 21.4, 62.9, 109.0, 114.2, 118.6, 119.6, 123.2, 126.4, 127.9, 128.6, 130.4, 134.5, 138.6, 154.1, 155.8. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{14}NO_3^+$ $[M + H]^+$ 256.0968; found 256.0963.

2-Hydroxy-5-methoxy-8,9-dimethylphenanthridin-6(5H)-one (**5i**). Yellowish solid (37.7 mg, 70%). Mp 216−217 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.38 (s, 3H), 2.44 (s, 3H), 3.98 (s, 3H), 7.10 (d, J = 7.5 Hz, 1H), 7.46 (d, J = 8.5 Hz, 1H), 7.75 (s, 1H), 8.08 (s, 1H), 8.14 (s, 1H), 9.63 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 19.9, 20.5, 62.9, 109.0, 114.1, 118.5, 119.6, 123.6, 124.4, 128.3, 128.8, 130.7, 138.0, 142.9, 154.0, 155.9. HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{16}NO_3^+$ $[M + H]^+$ 270.1125; found 270.1114.

2-Hydroxy-5-methoxybenzo[j]phenanthridin-6(5H)-one (**5j**). Yellowish solid (30.3 mg, 52%). Mp 208−209 °C. ^{1}H NMR (500 MHz, DMSO): δ 4.03 (s, 3H), 7.13 (d, J = 8.5 Hz, 1H), 7.50 (d, J = 9.0 Hz, 1H), 7.66 (s, 1H), 7.73 (s, 1H), 7.97 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 9.01 (d, J = 12.5 Hz, 2H), 9.72 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 62.9, 109.8, 114.4, 118.6, 120.1, 122.4, 124.6, 127.6, 128.8, 129.0, 129.1, 129.4, 129.6, 132.2, 135.2, 154.3, 156.2. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{14}NO_3^+$ $[M + H]^+$ 292.0968; found 292.0976.

2-Hydroxy-5-methoxy-3-methylphenanthridin-6(5H)-one (**5k**). Yellowish solid (29.1 mg, 57%). Mp 207−208 °C. ^{1}H NMR (500 MHz, DMSO): δ 2.32 (s, 3H), 4.01 (s, 3H), 7.42 (s, 1H), 7.63 (t, J = 7.5 Hz, 1H), 7.73 (s, 1H), 7.86 (t, J = 7.0 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 8.34 (d, J = 7.5 Hz, 1H), 9.66 (s, 1H). ^{13}C NMR (125 MHz, DMSO): δ 17.1, 62.9, 108.2, 114.8, 116.9, 122.6, 126.1, 128.2, 128.9, 129.2, 132.8, 133.4, 152.4, 155.9. HRMS (ESI-TOF) *m/z*: calcd for $C_{15}H_{14}NO_3^+$ $[M + H]^+$ 256.0968; found 256.0947.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02903.

Experimental procedures and analytical data for all new compounds (PDF)

X-ray structure and crystallographic data for compound **3h** (CIF)

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Notes

The authors declare no competing financial interest.

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