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Indium-Mediated Intramolecular Reaction of *N*-(2-Iodobenzoyl)azabenzonorbornadienes: A General Access to Dihydrobenzo[*c*]phenanthridinones

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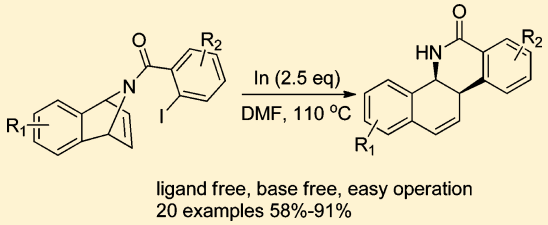
Supporting Information

ABSTRACT: An efficient synthesis of dihydrobenzo[*c*]phenanthridinones was achieved by utilizing an indium(0)-mediated intramolecular cyclization reaction under ligand- and base-free conditions. A variety of functional groups were tolerated in the present protocol.



INTRODUCTION

Benzo[*c*]phenanthridines are an important group of naturally occurring alkaloids that widely exist in Papaveraceae and Putaceae plants.[1] Many members of this family (Figure 1), such as chelidonine, chelamidine, chelamine, homochelidonine, sanguinarine, and nitidine, often possess various interesting biological activities,[2] which make them attractive targets for chemical and biological communities.[3−8] The synthesis of partially unsaturated dihydrobenzo[*c*]phenanthridine alkaloids of this family still remains challenging due to the existence of two contiguous chiral bridge carbon atoms. Among the previously described methods, much attention has been paid to the ring-opening reaction of azabenzonorbornadienes, resulting in benzo[*c*]phenanthridine skeletons. In particular, Lautens et al. reported a highly efficient synthesis of natural dihydrobenzo[*c*]phenanthridines using Pd-catalyzed ring-opening reactions of azabenzonorbornadienes with an aryl boronic acid as the key step.[4,5] Our group also developed an efficient method to construct dihydrobenzo[*c*]phenanthridinones through the ring-opening reaction of azabenzonorbornadienes with methyl *o*-iodobenzoates, which was successfully applied to the total synthesis of five natural benzo[*c*]phenanthridines[6−8] (Scheme 1). All of these reports involved an elaborate Pd catalytic system, and there were few studies on the intramolecular cyclization reaction of azabenzonorbornadienes. From a practical perspective, the ring-opening reaction of azabenzonorbornadienes with a cheaper metal and a simple reaction system is highly desirable.

As a relatively inexpensive metal, indium exhibits a low heterophilicity in many organic reactions, and thus oxygen- and nitrogen-containing functional groups are usually tolerated by these organoindium reagents. In the past few decades, indium-mediated organic reactions have elicited considerable attention. Most synthetically useful indium-mediated reactions are mainly limited to the Ferrier-type alkynylation reactions and allyl alkylation of carbonyl compounds and imine derivatives,[9,10] whereas few reports involved the indium-mediated ring-opening reaction of azabicyclic olefins.[11,12] Cheng and co-workers reported a Pd-catalyzed ring-opening process of azabicyclic olefins with organic halides via an abnormal Heck-type reaction.[13] Wang et al. reported an indium(III)-catalyzed Heck reaction and suggested that the organoindium intermediate, generated in situ from the reaction of phenyl iodide and indium salt, could easily react with styrene to provide the Heck reaction compound.[14] Recently, we also turned our interest to the indium-mediated Heck-type reactions. To this end, we envisaged that the ring-opening reaction of azabenzonorbornadienes could be promoted by an indium reagent.

Our continuous efforts on the synthesis of benzo[*c*]-phenanthridines[6−8] in combination with indium chemistry[15,16] has resulted in the development of a few new approaches to dihydrobenzo[*c*]phenanthridinones through a Pd-catalyzed intermolecular cascade reaction (Scheme 1). As a part of our ongoing project on indium chemistry, we herein report a new methodology for the synthesis of dihydrobenzo[*c*]-phenanthridines based on an intramolecular cyclization reaction of *N*-(2-iodobenzoyl)azabenzonorbornadienes.

RESULTS AND DISCUSSION

As we know, an organoindium reagent can be formed by treatment of aryl iodide with the indium(0) metal.[17] Thus, the substrates bearing an iodide group, *N*-(2-iodobenzoyl)-azabenzonorbornadiene **1a**, were prepared smoothly according to the previously reported methods.[18] With substrate **1a** in hand, we subsequently examined its behavior with indium metal. In our initial attempts, the reaction of **1a** with 1.5 equiv

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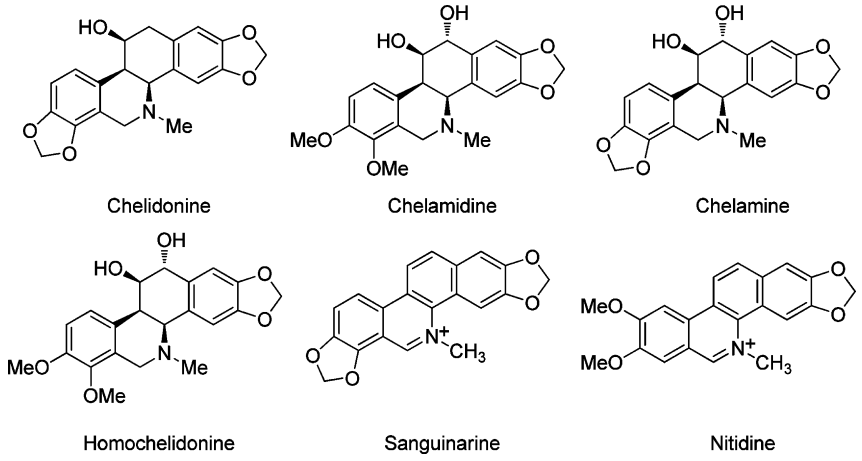
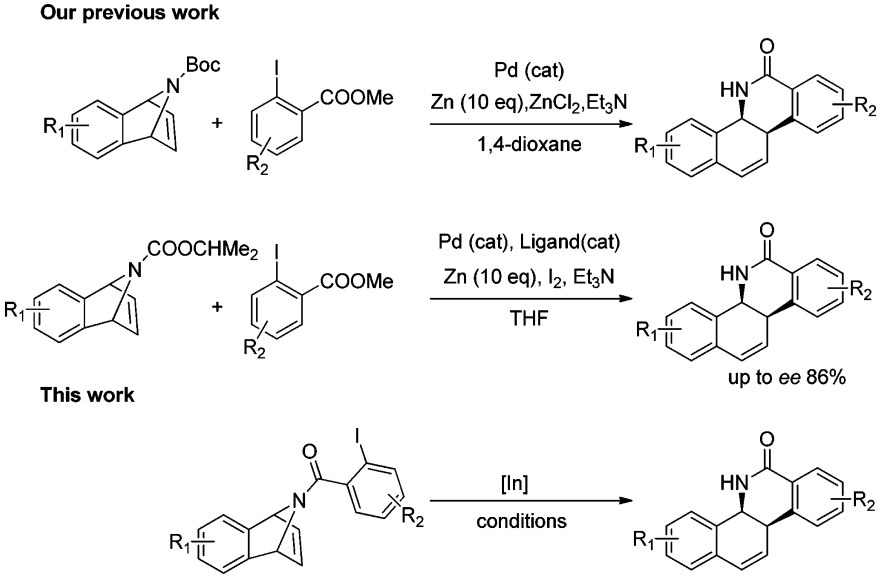


Figure 1. Naturally occurring benzo[*c*]phenanthridine alkaloids.

Scheme 1. Synthesis of Benzo[*c*]phenanthridines



of indium in the presence of 2.0 equiv of LiCl at 110 °C did not produce any desired product **2a** (entry 1, Table 1). To our delight, when LiCl was removed from the reaction system, the reaction produced **2a** in 52% yield with incomplete conversion of the starting material (entry 2, Table 1). Further studies have demonstrated that DMF proved to be the optimal solvent for this process (entries 8 and 9, Table 1), and other solvents such as toluene, dioxane, THF, DME, and methanol failed to provide the desired products (entries 11−14, Table 1). The molar quantity of the indium metal also significantly influenced the reaction efficacy. The highest yield was obtained with a 2.5 equiv of In(0) metal (entry 8, Table 1). Finally, the *cis*-stereochemistry of product **2a** was confirmed by X-ray diffraction crystallographic analysis (see the Supporting Information).[19]

Next, using the above-mentioned optimized reaction conditions, we examined the scope and limitations of this present protocol. The results are summarized in Table 2. A range of *N*-(2-iodobenzoyl)azabenzonorbornadienes **1b−1p** with various substituents in the aromatic ring were examined. Fifteen dihydrobenzo[*c*]phenanthridinones **2b−2p** were successfully obtained under the optimal conditions with a yield of 58−91% (entries 1−16, Table 2). Both the electron-donating and electron-withdrawing groups were tolerated in the present procedure. Related to the electronic properties in compounds **1**, the steric characteristics of the substrates significantly influenced the efficacy of the reactions. The substrates possessing a substituent adjacent to the iodide group generally gave a decreased yield (entries 2−4, Table 2). It is noteworthy that compounds **2o** and **2p** represent the mature precursors for naturally occurring alkaloids chelidonine and nitidine. Unfortunately, reactions with the corresponding aryl bromide and chloride did not yield the target benzo[*c*]phenanthridines (entries 17 and 18, Table 2).

To examine the generality of the present methodology, the chain-extending substrates *N*-(2-iodophenylacetyl)azabenzonorbornadiene derivatives **3** and *N*-(2-iodophenylpropionyl)-azabenzonorbornadiene **5** were also subject to the indium-mediated cyclization process, and the results are shown in Scheme 2. To our delight, under optimized reaction conditions, the reactions of phenylacetic acid-derived substrates **3a** and **3b** smoothly provided the desired products **4a** and **4b** in 84 and 91% yield, respectively. However, the 3-phenylpropanyl acid-

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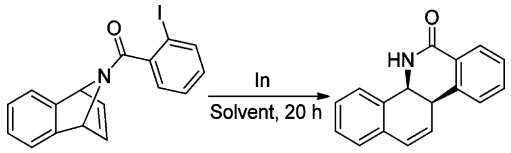
Table 1. Intramolecular Reaction of Compound 1a[a]



1a 2a

entry	In (equiv)	solvent	temp (°C)	yield (%)[b]
1[c]	1.5	DMF	110	0
2	1.5	DMF	110	52
3	1.5	DMF	120	49
4	1.5	DMF	130	51
5	1.5	DMF	140	52
6	1.0	DMF	110	33
7	2.0	DMF	110	70
8	2.5	DMF	110	84
9	3.0	DMF	110	84
10[d]	2.5	DMF	110	56
11	2.5	toluene	110	0
12	2.5	1,4-dioxane	110	0
13	2.5	THF	110	0
14	2.5	DME	110	0
15	2.5	DMSO	110	78
16	2.5	MeOH	110	21
17[e]	2.5	DMF	110	67

[a]Reaction conditions: **1a** (0.2 mmol), In, solvent (2.5 mL), 20 h, under an argon atmosphere. [b]Isolated yield. [c]In·LiCl was used. [d]Reaction time: 10 h. [e]1 mmol of **1a** was used.

derived *N*-(2-iodophenylpropionyl)azabenzonorbornadiene **5** proved to be an ineffective substrate.

Subsequently, regioselectivity of the present reaction was further studied (Scheme 3). For compounds **6a** and **6b** containing a methyl group in the bridgehead atom, two possible cyclization products might be afforded. Nevertheless, only regioisomers dihydrobenzo[*c*]phenanthridinones **7a** and **7b** were obtained in 72 and 63% yield, respectively. Unexpectedly, compound **6c**, which incorporates a methyl group at the double bond, did not supply the desired phenanthridine derivative under the optimal reaction conditions. It was presumed that the presence of the methyl group on the C−C double bond of olefin possibly hampered the coordination to the indium center generated in situ.

Based on the above-mentioned results and previously reported work,[13,14,17] a plausible mechanism for the synthesis of dihydrobenzo[*c*]phenanthridinones is putatively outlined in Scheme 4. At the outset, an organoindium intermediate **8** was formed in situ. The subsequent intramolecular insertion reaction into the carbon−carbon double bond of the olefin produced a cyclic intermediate **9**, which underwent a β-elimination/ring opening to give the full scaffold **10**. Finally, the protonation of **10** provided the benzophenanthridine **2a**.

CONCLUSION

In conclusion, we have described an efficient In(0)-mediated intramolecular cyclization strategy for the synthesis of dihydrobenzo[*c*]phenanthridinone derivatives from *N*-(2-iodobenzoyl)azabenzonorbornadienes. This present methodology was demonstrated to have wide functional group tolerance and high regioselectivity. Further investigation on the enantioselective synthesis of benzo[*c*]phenanthridinones utilizing this protocol is currently under development and will be reported in the future.

EXPERIMENTAL SECTION

Chemicals and solvents were purchased from commercial suppliers and used as received unless otherwise stated. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded with $CDCl_3$ or DMSO-d_6 as solvent. The chemical shifts are reported as δ values (ppm) relative to tetramethylsilane. HRMS spectra were recorded with a Q-TOF mass spectrometer, equipped with an ESI source. Melting points were determined with a melting point apparatus and are uncorrected.

General Procedure for Synthesis of Substrates 1a−1r, 3a, 3b, and 5. Compounds **1a−1r**, **3a**, **3b**, and **5** were synthesized according to the previously reported method.[18]

To *N*-Boc pyrrole (16.7 g, 100 mmol) in DME (40 mL) at 55 °C in a flame-dried three-neck flask fitted with a reflux condenser and two addition funnels was simultaneously added a solution of anthranilic acid (13.8 g, 100 mmol) in DME (100 mL) and a separate solution of isoamylnitrite (16.8 mL, 125 mmol) in DME (50 mL). The addition took about 45 min. The reaction was allowed to stir at 55 °C for 30 min until no further gas evolved. The crude red solution was reduced in volume by rotovap distillation to approximately one-half of the original volume. The reaction mixture was then partitioned between EtOAc and saturated K_2CO_3, and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The resulting dark brown oil was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 v/v) to give the *N*-Boc intermediate (13.85 g, 57%) as light yellow solid.

The *N*-Boc intermediate (600 mg, 2.4 mmol) was dissolved in 10 mL of DCM followed by the addition of Et_3N (0.4 mL) and heating to reflux. TMSI (0.4 mL, 2.6 mmol) was added dropwise over 5 min, and the reaction was heated at reflux for an additional 15 min, after which time TLC analysis showed complete consumption of the *N*-Boc intermediate. The reaction mixture was cooled to 0 °C, and MeOH (0.1 mL, 3 mmol) was added dropwise. After 10 min at 0 °C, 2-iodobenzoyl chloride (954 mg, 3.6 mmol) was added, and the reaction was allowed to warm to room temperature. The reaction was stirred at room temperature for an additional hour. Water (10 mL) and DCM were added until all precipitates dissolved. The organic and aqueous phases were separated, and the aqueous phase was extracted twice with DCM. The organic fractions were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1 v/v) to give compound **1a** (682 mg, 74%) as a white solid.

The rest of substrates **1b−1r**, **3a**, **3b**, and **5** were prepared by a procedure similar to that for **1a**.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(2-iodophenyl)-methanone (**1a**):* light yellow solid, 600 mg, 74%; mp 123−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, J = 7.9, 0.5 Hz, 1H), 7.36−7.32 (m, 2H), 7.17−7.05 (m, 4H), 7.02−6.92 (m, 3H), 6.09 (s, 1H), 5.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 147.9, 147.8, 143.7, 142.8, 140.8, 139.7, 130.9, 128.1, 127.6, 125.4, 125.2, 121.5, 120.6, 92.2, 66.7, 63.0; HRMS (ESI) m/z calcd for $C_{17}H_{12}INO$ $[M + H]^+$ 374.0042, found 374.0042.

*(3-Chloro-2-iodophenyl)(1,4-dihydro-1,4-epiminonaphthalen-9-yl)methanone (**1b**):* light yellow solid, 664 mg, 68%; mp 186−188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, J = 8.0, 1.5 Hz, 1H), 7.39 (d, J = 6.6 Hz, 1H), 7.33 (t, J = 7.7 Hz, 1H), 7.22−7.12 (m, 2H), 7.05−6.97 (m, 4H), 6.13 (s, 1H), 5.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.8, 146.7, 146.6, 142.9, 142.5, 141.7, 139.1, 128.8, 128.5, 124.4, 124.2, 124.1, 120.5, 119.6, 95.7, 65.4, 61.9; HRMS (ESI) m/z calcd for $C_{17}H_{11}ClINO$ $[M + H]^+$ 407.9652, found 407.9645.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(3-fluoro-2-iodophenyl)methanone (**1c**):* off white solid, 572 mg, 61%; mp 183−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.33 (m, 2H), 7.21−7.08 (m, 3H), 7.07−6.97 (m, 3H), 6.95 (d, J = 7.4 Hz, 1H), 6.12 (s, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (d, J = 2.3 Hz), 160.9 (d, J = 247.0 Hz), 146.6 (d, J = 14.0 Hz), 142.6, 142.0,

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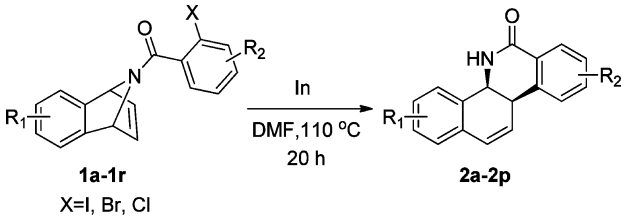
Table 2. Intramolecular Reaction of Compounds 1a−1r[a]



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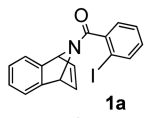
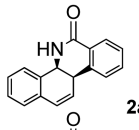
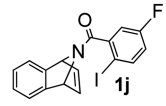
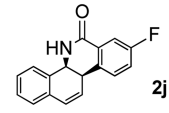
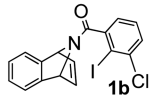
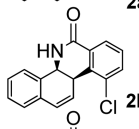
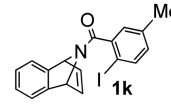
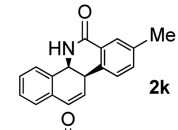
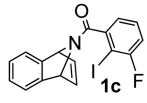
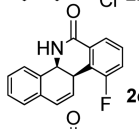
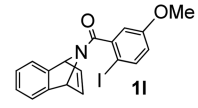
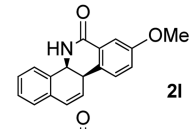
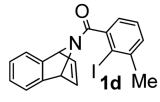
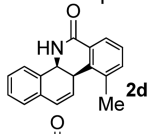
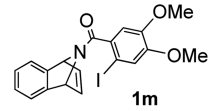
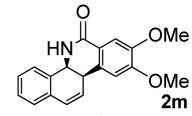
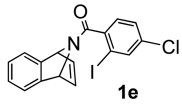
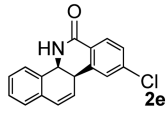
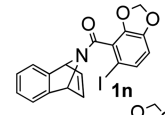
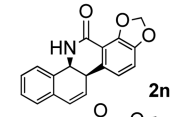
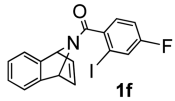
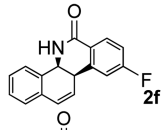
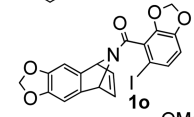
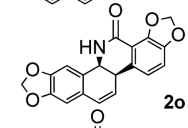
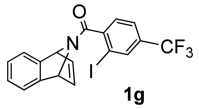
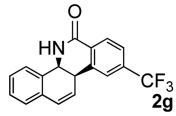
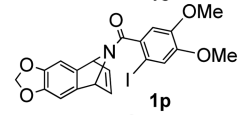
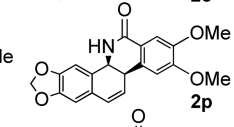
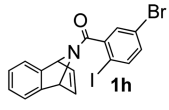
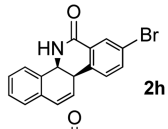
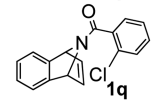
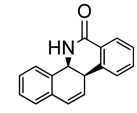
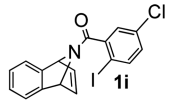
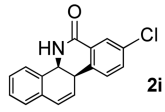
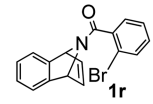
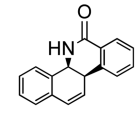
1	 1a	 2a	84	10	 1j	 2j	83
2	 1b	 2b	58	11	 1k	 2k	84
3	 1c	 2c	63	12	 1l	 2l	87
4	 1d	 2d	61	13	 1m	 2m	90
5	 1e	 2e	84	14	 1n	 2n	85
6	 1f	 2f	81	15	 1o	 2o	87
7	 1g	 2g	86	16	 1p	 2p	91
8	 1h	 2h	81	17	 1q	 2q	0
9	 1i	 2i	80	18	 1r	 2r	0

[a]Reaction conditions: **1** (0.2 mmol), In (0.5 mmol), DMF (2.5 mL), 110 °C, 20 h, under an argon atmosphere. [b]Isolated yield.

141.6, 129.3, 129.2, 124.3 (d, J = 14.8 Hz), 122.1 (d, J = 3.5 Hz), 120.5, 119.6, 115.2 (d, J = 24.6 Hz), 79.6 (d, J = 27.4 Hz), 65.6, 61.9; HRMS (ESI) m/z calcd for $C_{17}H_{11}FINO$ $[M + H]^+$ 391.9948, found 391.9948.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(2-iodo-3-methylphenyl)methanone (**1d**):* white solid, 669 mg, 72%; mp 153−155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 6.7 Hz, 1H), 7.28−7.22 (m, 2H), 7.15−7.11(m, 2H), 7.04−6.94 (m, 3H), 6.88 (s, 1H), 6.12 (s, 1H), 5.07 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 146.9, 141.9, 141.8, 141.0, 129.2, 127.1, 124.3, 124.1, 123.6, 120.4, 119.5, 97.8, 65.5, 61.8, 27.9; HRMS (ESI) m/z calcd for $C_{18}H_{14}INO$ $[M + H]^+$ 388.0198, found 388.0197.

*(4-Chloro-2-iodophenyl)(1,4-dihydro-1,4-epiminonaphthalen-9-yl)methanone (**1e**):* light yellow oil, 752 mg, 77%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.41−7.33 (m, 2H), 7.22−7.11 (m, 2H), 7.07 (d, J = 8.1 Hz, 1H), 7.04−6.97 (m, 3H), 6.09 (s, 1H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 147.8, 147.6, 143.7, 142.6, 139.3, 139.2, 135.8, 128.5, 128.4, 125.4, 125.3, 121.6, 120.6, 92.4, 66.8, 63.1; HRMS (ESI) m/z calcd for $C_{17}H_{11}ClINO$ $[M + H]^+$ 407.9652, found 407.9650.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(4-fluoro-2-iodophenyl)methanone (**1f**):* light yellow solid, 601 mg, 64%; mp 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 8.1, 2.3 Hz, 1H), 7.24 (d, 7.0 Hz, 1H), 7.07−6.92 (m, 4H), 6.91−6.81 (m, 3H), 5.95 (s, 1H), 4.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 161.2 (d, J = 254.5 Hz), 146.7 (d, J = 20.1 Hz), 142.7, 141.5, 136.0 (d, J = 3.6 Hz), 127.9 (d, J = 8.5 Hz), 125.9, 125.7, 124.4, 124.2, 120.5 119.5, 114.4 (d, J = 21.5 Hz), 91.1 (d, J = 8.2 Hz), 65.8, 62.0; HRMS (ESI) m/z calcd for $C_{17}H_{11}FINO$ $[M + H]^+$ 391.9948, found 391.9942.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(2-iodo-4-(trifluoromethyl)phenyl)methanone (**1g**):* light yellow solid, 751 mg, 71%, mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.38 (d, J = 6.6 Hz, 1H), 7.29−7.20 (m, 1H), 7.19−7.10 (m, 2H), 7.03−6.98 (m, 3H), 6.10 (s, 1H), 5.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 147.5 (d, J = 17.6 Hz), 144.4, 143.6, 142.6, 136.6 (q, J = 3.8 Hz), 132.7 (q, J = 33.1 Hz), 127.8, 125.5,

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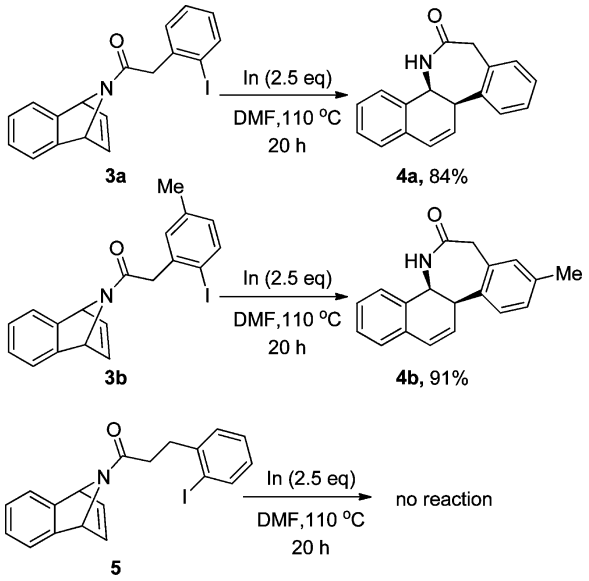
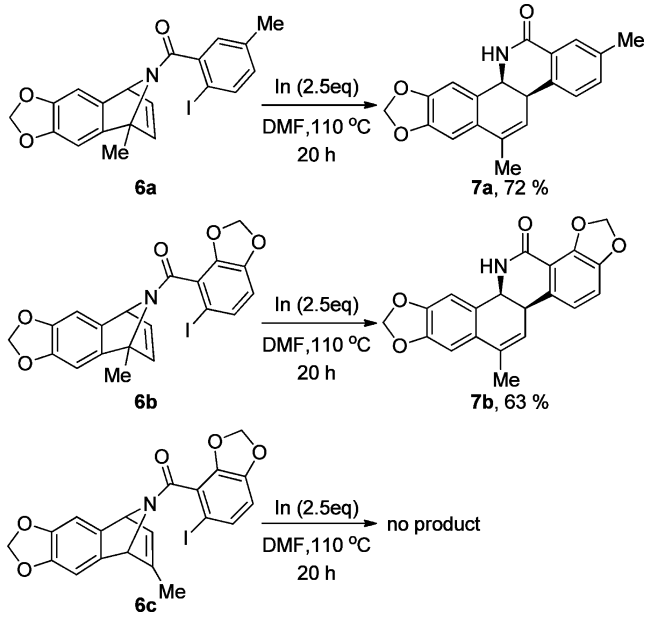
Scheme 2. Examination of the Substrate Scope



Scheme 3. Investigation of the Regioselectivity



125.4, 125.2 (q, J = 3.6 Hz), 123.9, 121.6, 121.2, 120.7, 92.0, 66.6, 63.0; HRMS (ESI) m/z calcd for $C_{18}H_{11}F_3INO$ $[M + H]^+$ 441.9916, found 441.9909.

*(5-Bromo-2-iodophenyl)(1,4-dihydro-1,4-epiminonaphthalen-9-yl)methanone (**1h**):* light yellow solid, 714 mg, 66%; mp 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.3 Hz, 1H), 7.35 (d, J = 7.1 Hz, 1H), 7.26−7.19 (m, 2H), 7.17 (d, J = 6.1 Hz, 1H), 7.11 (dd, J = 5.5, 2.4 Hz, 1H), 7.04−6.92 (m, 3H), 6.06 (s, 1H), 5.08 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 147.7, 147.5, 143.6, 142.7, 142.6, 141.1, 133.9, 130.6, 125.5, 125.3, 122.6, 121.6, 120.7, 90.1, 66.7, 63.0; HRMS (ESI) m/z calcd for $C_{17}H_{11}BrINO$ $[M + H]^+$ 451.9147, found 451.9138.

*(5-Chloro-2-iodophenyl)(1,4-dihydro-1,4-epiminonaphthalen-9-yl)methanone (**1i**):* off white solid, 713 mg, 73%; mp 128−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, J = 8.3 Hz, 1H), 7.41−7.37 (d, J = 7.0 Hz, 1H), 7.23−7.18 (d, J = 7.0 Hz, 1H), 7.18−7.08 (m, 3H), 7.07−6.98 (m, 3H), 6.10 (s, 1H), 5.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4, 146.6, 146.5, 142.6, 141.6, 141.3, 139.9, 133.7, 130.0, 126.7, 124.4, 124.3, 120.5, 119.7, 88.2, 65.6, 61.9; HRMS (ESI) m/z calcd for $C_{17}H_{11}ClINO$ $[M + H]^+$ 407.9652, found 407.9647.

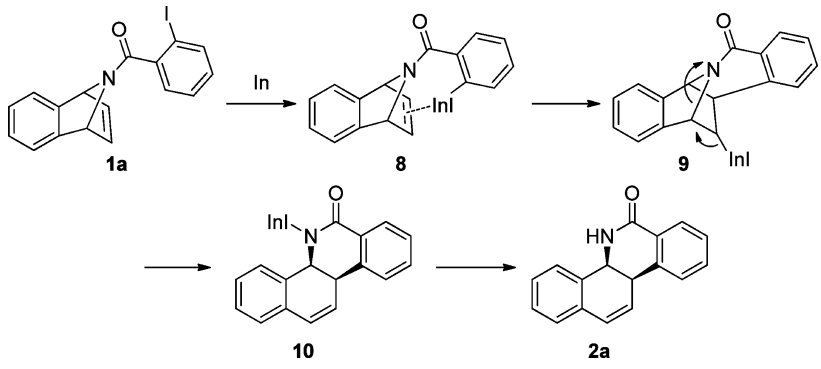
*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(5-fluoro-2-iodophenyl)methanone (**1j**):* off white solid, 535 mg, 57%; mp 152−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 9.2, 5.3 Hz, 1H), 7.39 (d, J = 6.3 Hz, 1H), 7.21 (d, J = 6.3 Hz, 1H), 7.16 (dd, J = 5.6, 2.5 Hz, 1H), 7.08−6.97 (m, 3H), 6.94−6.84 (m, 2H), 6.11 (s, 1H), 5.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, J = 250.3 Hz), 162.5, 147.7, 147.5, 143.6, 142.6, 142.5 (d, J = 6.3 Hz), 141.3 (d, J = 7.6 Hz), 125.5, 125.3, 121.6, 120.7, 118.5 (d, J = 21.7 Hz), 115.3 (d, J = 23.5 Hz), 85.2 (d, J = 3.5 Hz), 66.6, 63.0; HRMS (ESI) m/z calcd for $C_{17}H_{11}FINO$ $[M + H]^+$ 391.9948, found 391.9940.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(2-iodo-5-methylphenyl)methanone (**1k**):* white solid, 697 mg, 75%; mp 172−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 6.3 Hz, 1H), 7.09 (d, J = 6.4 Hz, 1H), 7.06 (dd, J = 5.6, 2.5 Hz, 1H), 6.98−6.89 (m, 3H), 6.89−6.81 (m, 2H), 6.02 (s, 1H), 5.03 (s, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 147.9, 147.9, 143.7, 142.8, 140.7, 139.4, 138.4, 131.9, 128.4, 125.3, 125.2, 121.5, 120.6, 87.9, 66.7, 62.9, 20.9; HRMS (ESI) m/z calcd for $C_{18}H_{14}INO$ $[M + H]^+$ 388.0198, found 388.0196.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(2-iodo-5-methoxyphenyl)methanone (**1l**):* white solid, 667 mg, 69%; mp 139−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.5 Hz, 1H), 7.38 (d, J = 6.6 Hz, 1H), 7.19 (d, J = 6.5 Hz, 1H), 7.15 (dd, J = 5.6, 2.5 Hz, 1H), 7.06−6.94 (m, 3H), 6.75−6.67 (m, 2H), 6.11 (s, 1H), 5.13 (s, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 158.7, 146.8, 146.7, 142.5, 141.7, 140.5, 139.4, 124.3, 124.2, 120.5, 119.6, 116.4, 112.2, 79.4, 65.6, 61.9, 54.5; HRMS (ESI) m/z calcd for $C_{18}H_{14}INO_2$ $[M + H]^+$ 404.0147, found 404.0145.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(2-iodo-4,5-dimethoxyphenyl)methanone (**1m**):* white solid, 655 mg, 63%; mp 172−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 6.7 Hz, 1H), 7.24 (s, 1H), 7.19 (d, J = 6.6 Hz, 1H), 7.15 (dd, J = 5.5, 2.3 Hz, 1H), 7.04−6.97 (m, 3H), 6.65 (s, 1H), 6.08 (s, 1H), 5.15 (s, 1H), 3.91 (s, 3H),

Scheme 4. Plausible Reaction Mechanism



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3.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 150.2, 149.2, 148.0, 147.9, 143.6, 142.7, 133.1, 125.3, 125.2, 121.8, 121.5, 120.5, 110.8, 80.8, 67.0, 63.1, 56.3, 56.1; HRMS (ESI) m/z calcd for $C_{19}H_{16}INO_3$ $[M + H]^+$ 434.0253, found 434.0252.

*(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)(5-iodobenzo[d][1,3]-dioxol-4-yl)methanone (**1n**):* white solid, 711 mg, 71%; mp 193−195 °C; ^{1}H NMR (400 MHz, DMSO) δ 7.40 (dd, J = 5.0, 2.8 Hz, 1H), 7.32 (d, J = 7.9 Hz, 1H), 7.28 (d, J = 5.0 Hz, 1H), 7.18 (dd, J = 5.5, 2.4 Hz, 1H), 7.09 (dd, J = 5.4, 2.4 Hz, 1H), 7.00−6.91 (m, 2H), 6.82 (d, J = 8.2 Hz, 1H), 5.99 (s, 3H), 5.33 (br s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 149.0, 148.4, 148.3, 145.4, 144.3, 143.9, 132.6, 125.4, 125.3, 121.5, 121.1, 111.6, 102.6, 82.4, 66.3, 62.8; HRMS (ESI) m/z calcd for $C_{18}H_{12}INO_3$ $[M + H]^+$ 417.9940, found 417.9935.

*(5,8-Dihydro-5,8-epiminonaphtho[2,3-d][1,3]dioxol-10-yl)(5-iodobenzo[d][1,3]dioxol-4-yl)methanone (**1o**):* white solid, 741 mg, 67%; mp 194−196 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.1 Hz, 1H), 7.19−7.09 (m, 1H), 7.05 (s, 1H), 6.95 (s, 1H), 6.80 (s, 1H), 6.63 (d, J = 8.2 Hz, 1H), 6.05−5.91 (m, 5H), 5.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 148.2, 145.3, 144.6, 144.6, 143.9, 143.3, 142.2, 141.9, 132.5, 121.9, 111.1, 104.9, 104.1, 102.2, 101.3, 81.0, 66.4, 62.8; HRMS (ESI) m/z calcd for $C_{19}H_{12}INO_5$ $[M + H]^+$ 461.9838, found 461.9828.

*(5,8-Dihydro-5,8-epiminonaphtho[2,3-d][1,3]dioxol-10-yl)(2-iodo-4,5-dimethoxyphenyl)methanone (**1p**):* white solid, 836 mg, 73%; mp 192−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (s, 1H), 7.14 (dd, J = 5.5, 2.4 Hz, 1H), 6.99 (dd, J = 5.4, 2.3 Hz, 1H), 6.95 (s, 1H), 6.76 (s, 1H), 6.66 (s, 1H), 5.98 (s, 1H), 5.96 (d, J = 1.3 Hz, 1H), 5.90 (d, J = 1.4 Hz, 1H), 5.06 (s, 1H), 3.89 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7, 149.2, 148.2, 143.6, 143.6, 142.9, 142.0, 141.3, 141.1, 132.0, 120.8, 109.8, 104.0, 103.1, 100.2, 79.9, 66.1, 62.1, 55.2, 55.1; HRMS (ESI) m/z calcd for $C_{20}H_{16}INO_5$ $[M + H]^+$ 478.0151, found 478.0147.

*(2-Chlorophenyl)(1,4-dihydro-1,4-epiminonaphthalen-9-yl)-methanone (**1q**):* brown oil, 526 mg, 78%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43−7.35 (m, J = 7.5, 4.6 Hz, 3H), 7.30 (t, J = 7.9 Hz, 1H), 7.24 (d, J = 7.3 Hz, 1H), 7.20−7.12 (m, 2H), 7.05−6.95 (m, 3H), 6.14 (s, 1H), 5.15 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 146.7, 142.8, 141.7, 133.6, 130.0, 129.7, 128.9, 127.3, 125.9, 124.3, 124.2, 120.4, 119.4, 65.5, 61.9; HRMS (ESI) m/z calcd for $C_{17}H_{12}ClNO$ $[M + H]^+$ 282.0686, found 282.0684.

*(2-Bromophenyl)(1,4-dihydro-1,4-epiminonaphthalen-9-yl)-methanone (**1r**):* brown oil, 577 mg, 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 7.9, 1.0 Hz, 1H), 7.39−7.24 (m, 3H), 7.21−7.14 (m, 2H), 7.12 (dd, J = 5.6, 2.5 Hz, 1H), 7.04−6.91 (m, 3H), 6.11 (s, 1H), 5.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 147.8, 143.7, 142.8, 136.9, 133.2, 130.9, 128.3, 127.5, 125.3, 125.2, 121.4, 120.5, 119.5, 66.6, 62.9; HRMS (ESI) m/z calcd for $C_{17}H_{12}BrNO$ $[M + H]^+$ 326.0181, found 326.0176.

*1-(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)-2-(2-iodophenyl)-ethanone (**3a**):* white solid, 715 mg, 77%; mp 159−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, J = 7.9, 0.8 Hz, 1H), 7.32 (d, J = 6.5 Hz, 1H), 7.24−7.15 (m, 2H), 7.13 (dd, J = 7.7, 1.4 Hz, 1H), 7.09 (dd, J = 5.6, 2.5 Hz, 1H), 7.03−6.90 (m, 4H), 5.97 (s, 1H), 5.61 (s, 1H), 3.83−3.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 148.2, 147.9, 143.9, 142.5, 139.4, 137.6, 130.2, 128.7, 128.4, 125.3, 125.0, 121.4, 120.4, 101.1, 65.8, 63.5, 45.9; HRMS (ESI) m/z calcd for $C_{18}H_{14}INO$ $[M + H]^+$ 388.0198, found 388.0197.

*1-(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)-2-(2-iodo-5-methylphenyl)ethanone (**3b**):* white solid, 674 mg, 70%; mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 6.8 Hz, 1H), 7.14−7.05 (m, 2H), 7.02−6.91 (m, 3H), 6.86 (s, 1H), 6.81−6.71 (m, 1H), 5.97 (s, 1H), 5.57 (s, 1H), 3.71 (s, 2H), 2.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 148.2, 148.0, 143.7, 142.5, 139.1, 138.4, 137.1, 131.0, 129.7, 125.2, 124.9, 121.4, 120.4, 96.9, 65.8, 63.5, 45.9, 20.8; HRMS (ESI) m/z calcd for $C_{19}H_{16}INO$ $[M + H]^+$ 402.0355, found 402.0354.

*1-(1,4-Dihydro-1,4-epiminonaphthalen-9-yl)-3-(2-iodophenyl)-propan-1-one (**5**):* brown oil, 683 mg, 71%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 5.8 Hz, 1H), 7.26−7.18 (m, 3H), 7.11−7.04 (m, 1H), 7.02−6.94 (m, 2H), 6.94−6.84 (m, 2H), 5.93 (s, 1H), 5.61 (s, 1H), 3.13−2.81 (m, 2H), 2.60−2.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 148.2, 147.9, 144.3, 143.5, 142.3, 139.5, 130.0, 128.6, 128.2, 125.3, 125.1, 121.4, 120.4, 100.1, 65.7, 63.3, 35.8, 34.1; HRMS (ESI) m/z calcd for $C_{19}H_{16}INO$ $[M + H]^+$ 402.0355, found 402.0352.

General Procedure for the Synthesis of Substrates 6a and 6b. Compounds **6a** and **6b** were synthesized according to the previously reported method.[4]

A mixture of dibromide (2.78 g, 10 mmol) and freshly distilled *N*-Boc 2-methylpyrrole (2.7 g, 15 mmol) in toluene (20 mL) was cooled to −78 °C. *n*-Butyllithium (1.6 M in hexane; 13.8 mL, 22 mmol) was added dropwise over a period of 1.5 h. The resulting bright orange solution was allowed to warm up to 25 °C over 3 h and then left for a further 17 h at 25 °C. The reaction mixture was then quenched with water, and the phases were separated. The aqueous layer was extracted with EtOAc, and the organic layers were combined, dried over Na_2SO_4, and concentrated to give brown oil. The resulting crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 20/1 v/v) to give 1-methyl-*N*-Boc intermediate (2.29 g, 76%) as a yellow oil.

1-Methyl-*N*-Boc intermediate (722 mg, 2.4 mmol) was dissolved in 10 mL of DCM followed by the addition of Et_3N (0.4 mL) and heating to reflux. TMSI (0.4 mL, 2.6 mmol) was added dropwise over 5 min, and the reaction was heated at reflux for an additional 15 min, after which time TLC analysis showed complete consumption of the 1-methyl-*N*-Boc intermediate. The reaction mixture was cooled to 0 °C, and MeOH (0.1 mL, 3 mmol) was added dropwise. After 10 min at 0 °C, *o*-iodobenzoyl chloride (1.0 g, 3.6 mmol) was added, and the reaction was allowed to warm to room temperature. The reaction was stirred at room temperature for an additional hour. Water (10 mL) and DCM were added until all precipitates dissolved. The organic and aqueous phases were separated, and the aqueous phase was extracted twice with DCM. The organic fractions were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1 v/v) to give compound **6a** (0.61 g, 57%) as a light yellow solid.

Substrate **6b** was prepared by a procedure similar to that for **6a**.

*(2-Iodo-5-methylphenyl)(5-methyl-5,8-dihydro-5,8-epimino-naphtho[2,3-d][1,3]dioxol-10-yl)methanone (**6a**):* light yellow solid, 610 mg, 57%; mp 279−281 °C; ^{1}H NMR (400 MHz, DMSO) δ 10.23 (s, 1H), 7.81 (d, J = 7.9 Hz, 1H), 7.52 (s, 1H), 7.47 (s, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 7.1 Hz, 1H), 7.07 (d, J = 7.4 Hz, 1H), 6.17 (s, 2H), 2.50 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 168.9, 147.9, 147.7, 143.7, 139.2, 138.3, 132.1, 131.9, 131.4, 130.2, 129.3, 126.4, 125.2, 122.1, 101.9, 101.3, 100.8, 89.9, 20.8, 19.9; HRMS (ESI) m/z calcd for $C_{20}H_{16}INO_3$ $[M + H]^+$ 446.0253, found 446.0249.

*(5-Iodobenzo[d][1,3]dioxol-4-yl)(5-methyl-5,8-dihydro-5,8-epiminonaphtho[2,3-d][1,3]dioxol-10-yl)methanone (**6b**):* off white solid, 730 mg, 64%; mp decomposed at 236 °C; ^{1}H NMR (400 MHz, DMSO) δ 10.41 (s, 1H), 7.51 (s, 1H), 7.44−7.32 (m, 3H), 7.24 (d, J = 7.5 Hz, 1H), 6.87 (d, J = 8.1 Hz, 1H), 6.20 (s, 2H), 6.17 (s, 2H), 2.57 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.9, 147.9, 147.5, 147.2, 145.1, 131.6, 131.6, 130.5, 129.7, 125.8, 124.8, 124.7, 121.4, 110.9, 102.2, 101.4, 100.9, 99.9, 82.8, 19.4; HRMS (ESI) m/z calcd for $C_{20}H_{14}INO_5$ $[M + H]^+$ 475.9995, found 475.9994.

General Procedure for the Synthesis of Substrate 6c. A mixture of dibromide (2.78 g, 10 mmol) and freshly distilled *N*-Boc-3-methylpyrrole (2.7 g, 15 mmol) in toluene (20 mL) was cooled to −78 °C. *n*-Butyllithium (1.6 M in hexane; 13.8 mL, 22 mmol) was added dropwise over a period of 1.5 h. The resulting bright orange solution was allowed to warm to 25 °C over 3 h and then left for a further 17 h at 25 °C. The reaction mixture was then quenched with water, and the phases were separated. The aqueous layer was extracted with EtOAc, and the organic layers were combined, dried over Na_2SO_4, and concentrated to give a brown oil. The resulting crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1 v/v) to give the 2-methyl-*N*-Boc intermediate (1.62 g, 63%) as a pink solid.

2-Methyl-*N*-Boc intermediate (722 mg, 2.4 mmol) was dissolved in 10 mL of DCM followed by the addition of Et_3N (0.4 mL) and

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heating to reflux. TMSI (0.4 mL, 2.6 mmol) was added dropwise over 5 min, and the reaction was heated at reflux for an additional 15 min, after which time TLC analysis showed complete consumption of the 1-methyl-*N*-Boc intermediate. The reaction mixture was cooled to 0 °C, and MeOH (0.1 mL, 3 mmol) was added dropwise. After 10 min at 0 °C, *o*-iodobenzoyl chloride (1.0 g, 3.6 mmol) was added, and the reaction was allowed to warm to room temperature. The reaction was stirred at room temperature for an additional hour. Water (10 mL) and DCM were added until all precipitates dissolved. The organic and aqueous phases were separated, and the aqueous phase was extracted twice with DCM. The organic fractions were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 10/1 v/v) to give compound **6c** (0.86 g, 57%) as a light yellow solid.

(5-Iodobenzo[d][1,3]dioxol-4-yl)(6-methyl-5,8-dihydro-5,8-epiminonaphtho[2,3-d][1,3]dioxol-10-yl)methanone (***6c***): light yellow solid, 860 mg, 57%; mp >300 °C; ^{1}H NMR (400 MHz, DMSO) δ 10.32 (s, 1H), 7.65 (d, J = 8.3 Hz, 1H), 7.53 (s, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.33 (s, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 8.2 Hz, 1H), 6.23 (s, 2H), 6.13 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 163.9, 148.3, 148.3, 147.2, 145.8, 132.5, 131.9, 130.4, 129.8, 128.1, 127.4, 126.6, 125.3, 111.5, 104.1, 102.7, 101.7, 100.4, 83.0, 19.2; HRMS (ESI) m/z calcd for $C_{20}H_{14}INO_5$ $[M + H]^+$ 475.9995, found 475.9992.

General Procedure for the Synthesis of Target Compounds 2a−2p, 4a, 4b, 7a, and 7b. To a solution of **1a** (74.6 mg, 0.2 mmol) in DMF (2.5 mL) was added In (57.5 mg, 0.5 mmol). The mixture was heated to 110 °C and stirred for 20 h. The mixture was poured into water and extracted with EtOAc. The organic fractions were combined, dried over Na_2SO_4, and concentrated. The resulting crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate = 4/1 v/v) to give compound **2a** (41.5 mg, 84%) as an off white solid.

The rest of substrates **2b−2p**, **4a**, **4b**, **7a**, and **7b** were prepared by a procedure similar to that for **2a**. The known compounds **2a−2m**, **2o**, and **2p** showed satisfactory spectroscopic data in agreement with those reported in the literature.[6,7]

13,14-cis-Dihydrobenzo[c]phenanthridin-6-one (***2a***): off white solid, 41.5 mg, 84%; mp 173−174 °C (lit.[7] 173−175 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, J = 7.7, 1.1 Hz, 1H), 7.53 (td, J = 7.5, 1.4 Hz, 1H), 7.39 (td, J = 7.6, 1.0 Hz, 1H), 7.35−7.25 (m, 4H), 7.16 (d, J = 7.2 Hz, 1H), 6.58 (dd, J = 9.6, 2.7 Hz, 1H), 5.81 (d, J = 2.6 Hz, 1H), 5.79 (d, J = 2.7 Hz, 1H), 5.76 (s, 1H), 4.87 (d, J = 5.7 Hz, 1H), 3.89 (dt, J = 5.4, 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 139.6, 133.0, 132.7, 131.9, 129.3, 128.6, 128.4, 128.0, 127.9, 127.7, 127.6, 127.3, 127.1, 127.1, 52.2, 38.7; HRMS (ESI) m/z calcd for $C_{17}H_{13}NO$ $[M + H]^+$ 248.1075, found 248.1074.

10-Chloro-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2b***): white solid, 32.5 mg, 58%; mp 183−184 °C (lit.[7] 182−184 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.7 Hz, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.30−7.26 (m, 2H), 7.23−7.08 (m, 3H), 6.53 (dd, J = 9.5, 2.9 Hz, 1H), 5.55 (d, J = 9.5 Hz, 1H), 5.27 (s, 1H), 4.72 (d, J = 5.1 Hz, 1H), 4.23 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 136.9, 133.6, 132.9, 132.8, 130.9, 129.9, 129.9, 128.6, 128.4, 128.4, 127.6, 127.4, 126.9, 126.9, 51.7, 36.7; HRMS (ESI) m/z calcd for $C_{17}H_{12}ClNO$ $[M + H]^+$ 282.0686, found 282.0680.

10-Fluoro-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2c***): white solid, 33.4 mg, 63%; mp 179−180 °C (lit.[7] 178−180 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 7.8 Hz, 1H), 7.48−7.38 (m, 2H), 7.37−7.30 (m, 2H), 7.28 (d, J = 4.5 Hz, 3H), 7.24 (d, J = 7.5 Hz, 1H), 6.64 (dd, J = 9.6, 3.1 Hz, 1H), 5.69 (d, J = 9.5 Hz, 1H), 5.31 (s, 1H), 4.86 (d, J = 5.3 Hz, 1H), 4.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 159.4 (d, J = 247.0 Hz), 132.7, 130.9, 129.8, 128.7 (d, J = 8.0 Hz), 128.4, 128.3, 127.6 (d, J = 8.6 Hz), 127.3, 127.3, 126.5 (d, J = 17.3 Hz), 123.9 (d, J = 3.3 Hz), 119.6 (d, J = 21.5 Hz), 51.8, 32.8, 32.7; HRMS (ESI) m/z calcd for $C_{17}H_{12}FNO$ $[M + H]^+$ 266.0981, found 266.0974.

10-Methyl-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2d***): white solid, 31.8 mg, 61%; mp 201−202 °C (lit.[7] 201−203 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7.6 Hz, 1H), 7.46−7.16 (m, 6H), 6.62 (dd, J = 9.5, 3.1 Hz, 1H), 5.59 (d, J = 9.5 Hz, 1H), 5.30 (s, 1H), 4.77 (d, J = 5.2 Hz, 1H), 4.03 (s, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 137.6, 135.0, 134.7, 132.8, 131.6, 129.7, 128.4, 128.3, 128.0, 127.7, 127.5, 127.3, 127.3, 126.2, 51.9, 35.9, 18.9; HRMS (ESI) m/z calcd for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1232, found 262.1229.

9-Chloro-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2e***): white solid, 47.2 mg, 84%; mp 203−204 °C (lit.[7] 202−204 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.3 Hz, 1H), 7.44−7.28 (m, 5H), 7.21 (d, J = 7.3 Hz, 1H), 6.65 (dd, J = 9.6, 2.5 Hz, 1H), 5.84 (dd, J = 9.6, 2.8 Hz, 1H), 5.59 (s, 1H), 4.90 (d, J = 5.5 Hz, 1H), 4.02−3.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 141.4, 139.0, 132.5, 131.9, 129.7, 129.4, 128.6, 128.1, 127.9, 127.6, 127.4, 127.3, 127.2, 126.6, 52.2, 38.4; HRMS (ESI) m/z calcd for $C_{17}H_{12}ClNO$ $[M + H]^+$ 282.0686, found 282.0675.

9-Fluoro-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2f***): white solid, 42.9 mg, 81%; mp 176−179 °C (lit.[7] 176−178 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, J = 8.5, 5.9 Hz, 1H), 7.38−7.26 (m, 3H), 7.19 (d, J = 7.2 Hz, 1H), 7.08 (td, J = 8.5, 2.2 Hz, 1H), 7.03 (d, J = 8.9 Hz, 1H), 6.65 (dd, J = 9.5, 2.0 Hz, 1H), 5.94 (s, 1H), 5.86 (dd, J = 9.5, 3.1 Hz, 1H), 4.91 (d, J = 5.6 Hz, 1H), 3.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 (d, J = 249.9 Hz), 164.3, 142.5 (d, J = 8.4 Hz), 132.6, 132.0, 130.9 (d, J = 9.4 Hz), 129.3, 128.5, 127.9, 127.5, 127.4, 127.2, 124.5 (d, J = 2.7 Hz), 114.9 (d, J = 21.8 Hz), 113.9 (d, J = 22.2 Hz), 52.3, 38.6; HRMS (ESI) m/z calcd for $C_{17}H_{12}FNO$ $[M + H]^+$ 266.0981, found 266.0975.

9-(Trifluoromethyl)-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2g***): white solid, 54.2 mg, 86%; mp 210−212 °C (lit.[7] 211−213 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.58 (s, 1H), 7.38−7.26 (m, 3H), 7.18 (d, J = 7.2 Hz, 1H), 6.64 (dd, J = 9.6, 2.4 Hz, 1H), 6.03 (s, 1H), 5.84 (dd, J = 9.5, 3.0 Hz, 1H), 4.91 (d, J = 5.7 Hz, 1H), 4.10−3.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 140.5, 134.6, 134.3, 132.5, 131.7, 131.2, 129.5, 128.7, 128.6, 128.1, 127.5, 127.3, 124.9, 124.6 (q, J = 3.5 Hz), 124.1 (q, J = 3.4 Hz), 122.2, 52.2, 38.5; HRMS (ESI) m/z calcd for $C_{18}H_{12}F_3NO$ $[M + H]^+$ 316.0949, found 316.0941.

8-Bromo-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2h***): white solid, 52.7 mg, 81%; mp 242−244 °C (lit.[7] 243−245 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, J = 2.0 Hz, 1H), 7.66 (dd, J = 8.1, 2.1 Hz, 1H), 7.41−7.32 (m, 1H), 7.30−7.27 (m, 2H), 7.21 (t, J = 8.4 Hz, 1H), 6.61 (dd, J = 9.6, 2.5 Hz, 1H), 5.78 (dd, J = 9.5, 2.8 Hz, 1H), 5.54 (s, 1H), 4.87 (d, J = 5.6 Hz, 1H), 3.89−3.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 137.4, 134.9, 131.5, 130.6, 129.9, 128.7, 128.5, 127.9, 127.5, 126.8, 126.7, 126.5, 126.3, 120.6, 51.2, 37.2; HRMS (ESI) m/z calcd for $C_{17}H_{12}BrNO$ $[M + H]^+$ 326.0181, found 326.0175.

8-Chloro-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2i***): white solid, 45.0 mg, 80%; mp 219−220 °C (lit.[7] 219−221 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 2.3 Hz, 1H), 7.49 (dd, J = 8.1, 2.3 Hz, 1H), 7.38−7.30 (m, 1H), 7.28 (dd, J = 4.0, 1.7 Hz, 2H), 7.26 (s, 1H), 7.17 (d, J = 7.3 Hz, 1H), 6.60 (dd, J = 9.6, 2.6 Hz, 1H), 5.78 (dd, J = 9.6, 2.8 Hz, 1H), 5.72 (s, 1H), 4.86 (d, J = 5.7 Hz, 1H), 3.89 (dd, J = 5.5, 2.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 137.9, 133.8, 133.0, 132.6, 131.7, 129.6, 129.5, 128.7, 128.6, 128.0, 127.9, 127.7, 127.5, 127.3, 52.2, 38.2; HRMS (ESI) m/z calcd for$C_{17}H_{12}ClNO$ $[M + H]^+$ 282.0686, found 282.0684.

8-Fluoro-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2j***): white solid, 44.0 mg, 83%; mp 223−225 °C (lit.[7] 222−225 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, J = 9.0, 2.8 Hz, 1H), 7.39−7.27 (m, 4H), 7.23 (td, J = 8.3, 2.8 Hz, 1H), 7.18 (d, J = 7.3 Hz, 1H), 6.59 (dd, J = 9.6, 2.6 Hz, 1H), 5.77 (dd, J = 9.5, 2.6 Hz, 1H), 5.70 (s, 1H), 4.86 (d, J = 5.7 Hz, 1H), 4.03−3.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J = 2.1 Hz), 162.2 (d, J = 246.6 Hz), 135.3 (d, J = 3.2 Hz), 132.6, 131.7, 130.0 (d, J = 7.5 Hz), 129.5, 128.9 (d, J = 7.5 Hz), 128.5, 128.3, 127.6, 127.5, 127.2, 120.1 (d, J = 22.0 Hz), 114.7 (d, J = 23.1 Hz), 52.4, 38.1; HRMS (ESI) m/z calcd for $C_{17}H_{12}FNO$ $[M + H]^+$ 266.0981, found 266.0975.

8-Methyl-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (***2k***): white solid, 43.8 mg, 84%; mp 196−199 °C (lit.[7] 196−198 °C); ^{1}H

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NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.27 (ddd, J = 11.0, 7.5, 3.6 Hz, 2H), 7.21 (d, J = 5.2 Hz, 2H), 7.16 (d, J = 7.7 Hz, 1H), 7.11 (d, J = 7.3 Hz, 1H), 6.51 (dd, J = 9.6, 2.7 Hz, 1H), 5.72 (dd, J = 9.5, 2.5 Hz, 1H), 5.43 (s, 1H), 4.79 (d, J = 5.7 Hz, 1H), 3.96−3.62 (m, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 137.6, 136.6, 133.9, 132.8, 131.9, 129.4, 128.9, 128.4, 128.3, 127.7, 127.6, 127.1, 52.4, 38.4, 21.1; HRMS (ESI) m/z calcd for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1232, found 262.1228.

*8-Methoxy-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (**2l**):* white solid, 48.2 mg, 87%; mp 183−185 °C (lit.[7] 182−184 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 2.8 Hz, 1H), 7.38−7.32 (m, 1H), 7.30−7.28 (m, 1H), 7.26 (d, J = 8.4 Hz, 1H), 7.19 (d, J = 7.3 Hz, 1H), 7.12 (dd, J = 8.4, 2.8 Hz, 1H), 6.59 (dd, J = 9.6, 2.7 Hz, 1H), 5.79 (dd, J = 9.5, 2.3 Hz, 1H), 5.51 (s, 1H), 4.87 (d, J = 5.7 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 159.2, 132.8, 131.9, 131.6, 129.4, 129.1, 128.9, 128.4, 128.3, 127.7, 127.1, 127.0, 120.7, 111.1, 55.6, 52.5, 38.1; HRMS (ESI) m/z calcd for $C_{18}H_{15}NO_2$ $[M + H]^+$ 278.1181, found 278.1177.

*8,9-Dimethoxy-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (**2m**):* white solid, 55.3 mg, 90%; mp 238−240 °C (lit.[7] 238−241 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.44 (s, 1H), 7.32−7.26 (m, 2H), 7.21 (td, J = 7.5, 1.2 Hz, 1H), 7.11 (d, J = 7.4 Hz, 1H), 6.73 (s, 1H), 6.57 (dd, J = 9.6, 2.3 Hz, 1H), 5.77 (dd, J = 9.6, 3.3 Hz, 1H), 4.87 (d, J = 6.3 Hz, 1H), 3.95 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 153.3, 147.5, 132.8, 131.3, 129.4, 128.5, 127.8, 127.1, 126.7, 126.0, 125.9, 117.1, 109.5, 108.1, 55.3, 55.2, 51.6, 36.1; HRMS (ESI) m/z calcd for $C_{19}H_{17}NO_3$ $[M + H]^+$ 308.1287, found 308.1285.

*7,8-Methylenedioxy-13,14-cis-dihydrobenzo[c]phenanthridin-6-one (**2n**):* white solid, 49.5 mg, 85%; mp 236−238 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38−7.31 (m, 1H), 7.29 (t, J = 1.8 Hz, 2H), 7.18 (d, J = 7.3 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.59 (dd, J = 9.6, 2.6 Hz, 1H), 6.15 (dd, J = 6.7, 1.1 Hz, 2H), 5.80 (dd, J = 9.5, 2.6 Hz, 1H), 5.63 (s, 1H), 4.82 (d, J = 5.4 Hz, 1H), 3.92−3.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 148.3, 147.9, 132.9, 132.7, 131.9, 129.3, 129.2, 128.3, 127.5, 127.3, 127.1, 119.7, 111.9, 111.5, 102.5, 52.7, 38.7, 29.7; HRMS (ESI) m/z calcd for $C_{18}H_{13}NO_3$ $[M + H]^+$ 292.0974, found 292.0972.

*7,8-Methylenedioxy-13,14-cis-dihydrobenzodioxolebenzo[c]-phenanthridin-6-one (**2o**):* white solid, 58.3 mg, 87%; mp decomposed at 260 °C (lit.[7] decomposed at 260 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 (d, J = 7.9 Hz, 1H), 6.79−6.73 (m, 2H), 6.66 (s, 1H), 6.44 (dd, J = 9.5, 2.5 Hz, 1H), 6.14 (dd, J = 8.4, 1.2 Hz, 2H), 5.98 (s, 2H), 5.69 (dd, J = 9.5, 2.6 Hz, 1H), 5.64 (s, 1H), 4.70 (d, J = 5.5 Hz, 1H), 3.76 (dt, J = 5.5, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 148.3, 148.0, 147.9, 147.2, 133.0, 127.4, 127.3, 127.1, 119.6, 111.8, 111.4, 108.3, 107.7, 102.6, 101.4, 52.8, 38.6, 29.7; HRMS (ESI) m/z calcd for $C_{19}H_{13}NO_5$ $[M + Na]^+$ 358.0691, found 358.0689.

*8,9-Dimethoxy-13,14-cis-dihydrobenzodioxolebenzo[c]-phenanthridin-6-one (**2p**):* white solid, 63.9 mg, 91%; mp decomposed at 270 °C (lit.[7] decomposed at 270 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 6.79 (s, 1H), 6.76 (s, 1H), 6.68 (s, 1H), 6.47 (dd, J = 9.5, 2.6 Hz, 1H), 6.00 (dd, J = 2.6, 1.3 Hz, 2H), 5.70 (dd, J = 9.5, 2.6 Hz, 1H), 5.51 (s, 1H), 4.77 (d, J = 5.8 Hz, 1H), 3.97 (s, 3H), 3.95 (s, 3H), 3.84−3.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2, 151.9, 147.4, 147.0, 146.2, 132.2, 126.3, 125.9, 125.7, 124.9, 119.5, 108.9, 108.1, 107.4, 106.7, 100.3, 55.1, 51.7, 37.4; HRMS (ESI) m/z calcd for $C_{20}H_{17}NO_5$ $[M + Na]^+$ 374.1004, found 374.0996.

*7,13-cis-Dihydro-1H-benzo[d]naphtho[1,2-b]azepin-2-one (**4a**):* white solid, 43.8 mg, 84%; mp 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.09 (m, 8H), 6.71 (dd, J = 9.5, 2.9 Hz, 1H), 6.02 (d, J = 8.6 Hz, 1H), 5.44 (s, 1H), 5.01 (t, J = 4.2 Hz, 1H), 4.24 (d, J = 15.3 Hz, 1H), 4.11 (s, 1H), 3.77 (d, J = 15.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 137.9, 133.5, 132.5, 132.1, 131.6, 130.8, 130.2, 129.3, 128.2, 127.8, 127.7, 127.7, 127.4, 127.0, 53.5, 43.9, 42.5; HRMS (ESI) m/z calcd for $C_{18}H_{15}NO$ $[M + H]^+$ 262.1232, found 262.1227.

*5-Methyl-7,13-cis-dihydro-1H-benzo[d]naphtho[1,2-b]azepin-2-one (**4b**):* white solid, 50.1 mg, 91%; mp 149−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42−7.35 (m, 1H), 7.29 (d, J = 8.4 Hz, 3H), 7.24 (d, J = 7.3 Hz, 1H), 7.20 (d, J = 7.8 Hz, 1H), 7.13 (d, J = 7.8 Hz, 1H), 7.01 (s, 1H), 6.69 (dd, J = 9.5, 2.7 Hz, 1H), 6.00 (d, J = 9.4 Hz, 1H), 5.44 (s, 1H), 4.98 (t, J = 4.3 Hz, 1H), 4.20 (d, J = 15.2 Hz, 1H), 4.07 (s, 1H), 3.71 (d, J = 15.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 135.9, 133.7, 132.5, 131.5, 131.3, 130.4, 130.2, 129.0, 128.2, 127.5, 127.1, 126.7, 126.4, 125.9, 52.5, 42.4, 41.4, 19.8; HRMS (ESI) m/z calcd for $C_{19}H_{17}NO$ $[M + H]^+$ 276.1388, found 276.1384.

*8,12-Dimethyl-13,14-cis-dihydrobenzodioxolebenzo[c]-phenanthridin-6-one (**7a**):* light yellow solid, 45.9 mg, 72%; mp 232−234 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.33 (d, J = 7.5 Hz, 1H), 7.17 (d, J = 7.7 Hz, 1H), 6.86 (s, 1H), 6.78 (s, 1H), 5.98 (s, 1H), 5.53 (s, 1H), 5.47 (s, 1H), 4.69 (d, J = 5.4 Hz, 1H), 3.75 (s, 1H), 2.39 (s, 1H), 2.02 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 147.2, 145.8, 136.3, 136.2, 132.7, 130.5, 128.2, 127.3, 126.6, 125.9, 125.4, 122.9, 107.3, 103.9, 100.3, 51.9, 37.3, 20.1, 18.3; HRMS (ESI) m/z calcd for $C_{20}H_{18}NO_3$ $[M + H]^+$ 320.1287, found 320.1285.

*7,8-Methylenedioxy-12-methyl-13,14-cis-dihydrobenzodioxo-lebenzo[c]phenanthridin-6-one (**7b**):* light yellow solid, 44.0 mg, 63%; mp 244−246 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.91 (d, J = 7.8 Hz, 1H), 6.86 (s, 1H), 6.78 (s, 1H), 6.72 (d, J = 7.9 Hz, 1H), 6.13 (d, J = 9.1 Hz, 1H), 5.99 (s, 1H), 5.48 (s, 1H), 4.65 (d, J = 5.3 Hz, 1H), 3.71 (s, 1H), 2.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1, 147.2, 146.8, 145.9, 132.6, 130.7, 128.2, 125.3, 123.1, 118.6, 110.7, 110.4, 107.2, 104.0, 101.5, 100.4, 52.2, 37.7, 28.7, 18.3; HRMS (ESI) m/z calcd for $C_{20}H_{16}NO_5$ $[M + H]^+$ 350.1028, found 350.1024.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00839.

X-ray data for **2a** (CIF)

X-ray crystallography data, NMR spectra, HRMS (PDF)

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Notes

The authors declare no competing financial interest.

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