Synthesis of Lycorines by Intramolecular Aryne Cycloadditions†

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Lycorines and related compounds were obtained by a short and convergent method, based on an intramolecular Diels–Alder reaction between an azadiene and an aryne, both generated in situ.

Introduction

The lycorine alkaloids are a group of compounds (characterized by the skeleton **1**) isolated from Amaryllidaceae plants.[1] This group has attracted the attention of chemists and pharmacologists due to the interesting properties of some of its members. For example, hippadine inhibits fertility in mice,[2] lycorine and some derivatives show antiviral and antineoplasic activity,[3] anhydrolycorinium chloride shows activity against P-388 leukemia,[3a] and ungeremine[4] and kalbretorine[5] are active against several types of tumors (Figure 1).

Several procedures for the synthesis of individual lycorines have been developed,[1,6] but a short and efficient general method is not yet available. We realized that the lycorine skeleton **2** could be disconnected as shown in Scheme 1 to afford **3**, an aryne linked to an azadiene by a two-carbon chain. Intramolecular Diels–Alder reaction between the aryne and azadiene components of a key intermediate based on **3** should afford the tetracyclic skeleton of lycorines.[7]

For generation of the aryne–azadiene we proposed base-promoted dehydrohalogenation of an haloarene **4**

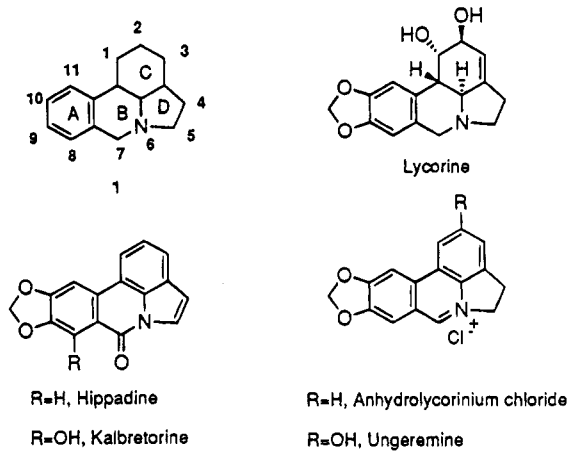
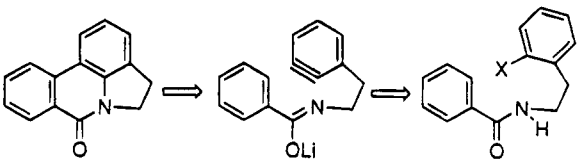


Figure 1.

Scheme 1



and, in the same basic medium, enolization of an amide. We now report the results of this approach.[8]

Results and Discussion

Amide intermediates **5** were prepared in excellent yields from the appropiate amines and acid chlorides using standard procedures (see supporting information). Subsequently, treatment of solutions of these amides with LDA or LTMP to generate the aryne and enolate functions gave one or more of the compounds shown in Scheme 2, the precise nature of the reaction product(s) depending on the substitution pattern in amide **5**, the reaction conditions (equivalents and concentrations of reactants, temperature, etc.), and the workup. Table 1 summarizes the results obtained for amides **5a–n**.

For the simplest amide, **5a**, the best results were obtained when 2.8 equiv of a 0.28 M solution of LDA or LTMP in THF was slowly added (syringe pump) to a cooled (−60 °C) 3.7 M solution of amide in THF. Under these conditions, we observed clean (TLC) formation of an adduct identified as **11a**. However, isolation of the

† Dedicated to the memory of Prof. Francisco Fariña.

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Scheme 2

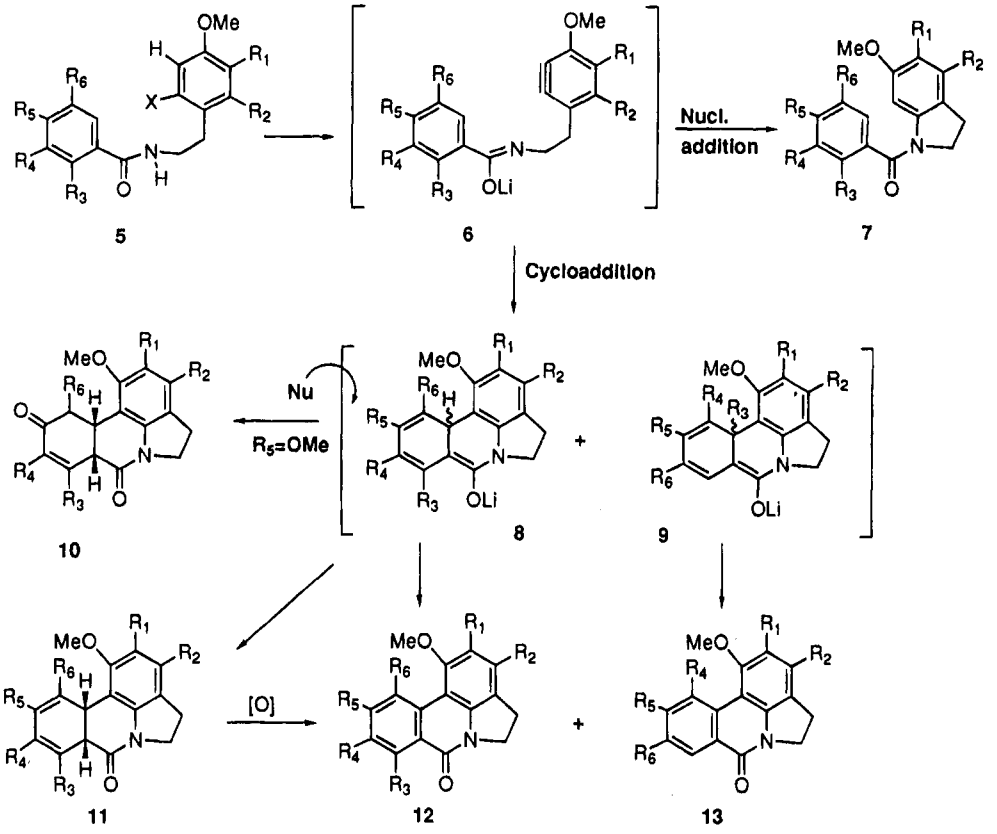


Table 1. Results of the Cyclization of Amides 5a–n

Entry	5	X	R_1	R_2	R_3	R_4	R_5	R_6	condns[a]	products (yields, %)		
1	**a**	Br	OMe	H	H	H	H	H	a	**12a** (32)		**11a** (37)
2	**a**	Br	OMe	H	H	H	H	H	b	**12a** (91)		
3	**b**	Br	OMe	H	OMe	OMe	H	H	b	**12b** (10)	**13b** (60)	
4	**c**	Br	OMe	H	OMe	OMe	OMe	H	a			**10c** (61)
5	**c**	Br	OMe	H	OMe	OMe	OMe	H	b	**12c** (69)	**13c** (10)	
6	**d**	Br	OMe	H	H	H	OMe	H	b	**12d** (76)	**13d** (10)	
7	**e**	Cl	H	H	H	H	OMe	H	b	**12e** (36)	**13e** (7)	**7e** (22)
8	**f**	Cl	H	H	OMe	OMe	OMe	H	b	**12f** (61)	**13f** (17)	
9	**f**	Cl	H	H	OMe	OMe	OMe	H	c	**12f'** (45)	**13f'** (11)	**7f'** (10)
10	**g**	Br	OMe	OMe	OMe	OMe	OMe	OMe	b	**12g** (43)	**13g** (11)	
11	**h**	Br	OMe	H	OMe	H	OMe	OMe	a		**13h** (13)	**10h** (43)
12	**h**	Br	OMe	H	OMe	H	OMe	H	c	**12h'** (35)	**13'** (17)	
13	**i**	Br	OMe	H	H	OCH_2O		H	b		**13i** (38)	
14	**j**	Br	OMe	H	OMe	OCH_2O		H	b	**12j** (17)	**13j** (58)	
15	**k**	Br	OMe	H	TMS	OCH_2O		H	a		**13k** (11)	**7k** (47)
16	**l**	Br	OMe	H	OH	OMe	H	H	d			**7l** (50)
17	**l**	Br	OMe	H	OH	OMe	H	H	e	**12l** (25)		
18	**m**	Br	OMe	H	OH	OMe	OMe	H	a	**12m** (20)		**7m** (51)
19	**m**	Br	OMe	H	OH	OMe	OMe	H	e	**12m** (36)		**7m** (18)
20	**n**	Br	OMe	H	OH	OCH_2O		H	a	**12n** (10)		**7n** (52)
21	**n**	Br	OMe	H	OH	OCH_2O		H	e	**12n** (30)		

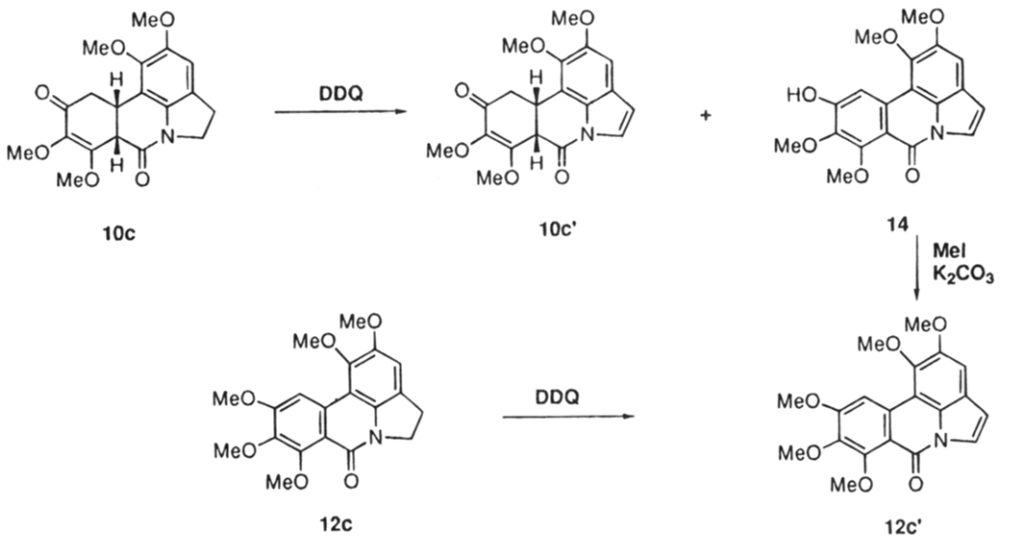
[a] Key: (a) (i) LDA or LTPM; (b) (i) LDA or LTPM, (ii) air; (c) (i) LDA or LTPM, (ii) DDQ; (d) (i) LDA, $B(OMe)_3$, (ii) LDA or LTMP; (e) (i) Ph_2SiCl_2, Et_3N, (ii) LDA or LTMP.

pure product was hampered by its gradual oxidation to **12a**, probably by atmospheric oxygen during workup. Scheme 2 includes a possible mechanism for the reaction which involves formation of an intermediate, **6a**, intramolecular Diels–Alder cycloaddition to **8a** (in this case **8a** = **9a**), tautomerization to **11a**, and oxidation to **12a**. To avoid the tedious purification of **11a**, we bubbled air through the crude reaction mixture and obtained **12a** in 91% yield.

Next, we examined the reaction of unsymmetrically substituted amides, which can lead to two regioisomers (entries 3–15, Table 1). For example, when amide **5b** was treated with LDA and air oxidized, compounds **12b** (10%) and **13b** (60%) were obtained. We assume that **12b** was formed by cyclization of **5b** to intermediate **8b**, followed by oxidation of **11b**, while formation of **13b** involved cyclization *ipso* to the MeO group of **5b**, to afford **9b**, followed by protonation and elimination of methanol.

When amide **5c** was cyclized (entry 4, Table 1), especially if a larger excess of base was used, we isolated a new compound which showed rather complex ^1H and ^{13}C NMR spectra. These presented signals corresponding only to four MeO groups (one less than the starting material), an aromatic proton, and a new methylene group. NOE experiments and $^1H-^{13}C$ correlations were necessary to establish the structure of this compound as

Scheme 3



10c. Presumably, this keto-amide was formed from enolate **8c** by nucleophilic attack on the methyl group of R_5 (CH_3O), followed by C-protonation of the resulting enolate to yield **10c** (Scheme 2). We assume that demethylation takes place during workup, since pretreatment of the crude reaction mixture with air allowed isolation of compounds **12c** (69%) and **13c** (10%) instead. To prove structure **10c** we planned a two-step transformation of **10c** into **12c** involving aromatization of ring A by oxidation with DDQ, followed by methylation of the phenol. However, treatment with DDQ produced aromatization of ring D to give the indole derivative **10c'** (84% yield) and traces of phenol **14**. Methylation of **14** with MeI/K_2CO_3 gave **12c'**, which was identical to the product obtained by DDQ oxidation of **12c** (Scheme 3).

Examination of the results in Table 1 revealed that small variations in the nature and/or position of the substituents led to different products, primarily as a result of changes in regioselectivity. For example, cyclization of 3,4-dimethoxybenzamide derivative **5d** (entry 6 in Table 1) went via **8d** to give the lycorine substituted in positions 9 and 10 (**12d**) as major product, while cyclization of 3,4-(methylenedioxy)benzamide derivative **5i** (entry 13) gave 10,11-substituted lycorine **13i** via **9i**, and cyclization of 2-methoxy-3,4-(methylenedioxy)benzamide derivative **5j** (entry 14) went mainly via **9j**, which lost a methoxy group to afford the 11-substituted lycorine **13j**.

In order to understand the factors governing the regioselectivity of the cyclization we considered the possible mechanisms occurring. We believe that the cyclization takes place via a two-step ionic mechanism that begins with nucleophilic attack on the benzyne by the nitrogen atom and then intramolecular addition of the phenyl carbanion to the activated benzene ring. However, an asynchronous concerted mechanism could not be ruled out. We also used MNDO calculations on model compounds[9] to estimate some electronic properties

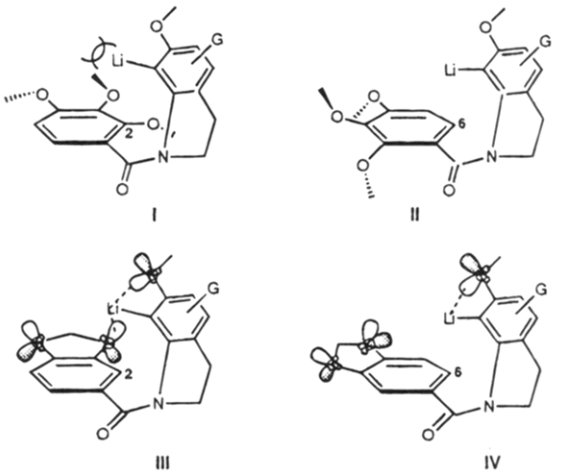


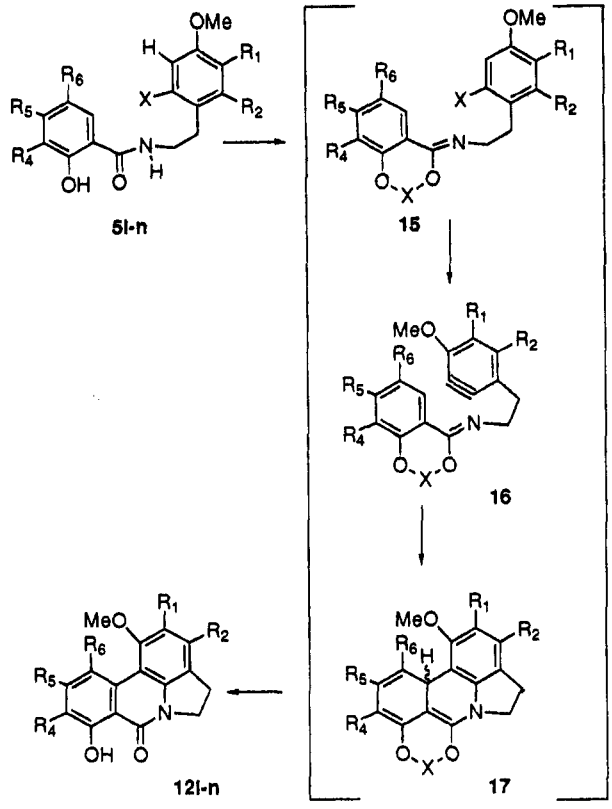
Figure 2.

of these amides and enolates but could not find a simple correlation between electronic effects and the regioselectivity of the cyclization. Steric effects may play an important role in determining the cyclization products, particularly in amides such as **5c** with three methoxy groups. In these derivatives cyclization can take place by approach of ring D either to position 2, occupied by a methoxy group, or to position 6 (structures I and II, respectively, Figure 2). However, because the three adjacent methoxy groups arrange themselves so as to minimize nonbonding interactions with each other, approach of ring D to position 2 is hindered by the methoxy group at position 3. Cyclization to position 6 is therefore favored, since it occurs via a less crowded transition state. Figure 2 shows these steric interactions for a stepwise mechanism, but those for a concerted mechanism should be very similar.

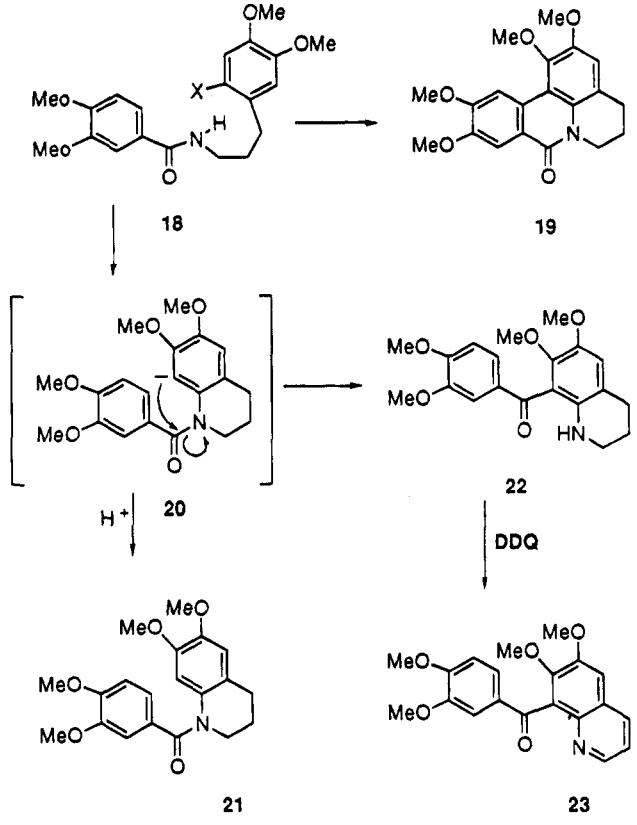
There is a further steric effect which may help to explain the results observed for the cyclization of methylenedioxy-substituted benzamides. The oxygen atoms of the methylenedioxy group lie roughly in the plane of the aromatic ring and so present only a minor steric hindrance to the approach of the nucleophilic D ring to position 2 (III, Figure 2). Furthermore, the nonbonding orbitals of these oxygens are oriented in such a way that they can coordinate to the lithium and thus favor the formation of **13**.

(9) Calculations were carried out for model compounds trying to establish some correlation between electronic factors and the regiochemistry of the cyclization. For amides **5b**, **5d**, **5e**, and **5j**, the position of cyclization corresponded to the position (2 or 6) with the larger coefficient in the LUMO of the corresponding model compound. However, for amides **5c**, **5f**, and **5g** the difference between these coefficients is not sufficiently large to account for the observed regioselectivy; for **5h** and **5i** the regioselectivy of the cyclization is just the opposite of that suggested by these calculations.

Scheme 4



Scheme 5



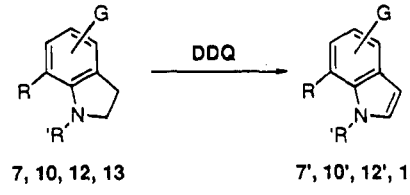
We believe that a delicate balance of all the above factors controls the course of the cyclization reaction, although solvent effects and the formation of dimers, trimers, etc., may also play a role.

Either way the course of the reaction was not easily predicted, so we tried to force cyclization to position 6 by protection of position 2 with a TMS group. However, when amide **5k** (entry 15) was treated with LDA, dihydroindole **7k** (47% yield) and a small amount of the C-2 cyclized product **13k** (11%) were isolated.

Some pharmacologically important lycorines have an OH group in position 8 (e.g., kalbretorine, Figure 1). We were therefore interested in the cyclization of amides **5l-n**. Attempts to cyclize phenolic amides **5m** and **5n** using LDA or LTMP alone were unsuccessful, leading to compounds **7m** and **7n**, respectively, via nucleophilic addition. In order to favor cyclization to position 6, we tried establishing a temporary connection between the hydroxy group in position 2 and the enolate oxygen using boron or silicon derivatives (Scheme 4). However, when **5l** was treated with LDA (excess) and $B(OMe)_3$ to generate the bridged compound **15** (X = BOMe) and then LDA to generate the aryne, **7l** was obtained in 50% yield. We considered that this result was due to the low stability of the boron intermediate under the reaction conditions and that the life of the bridged intermediate might be lengthened if a hindered silicon atom were used as bridge instead of boron. When amide **5l** was treated with Et_3N and Ph_2SiCl_2 to generate **15** (X = $SiPh_2$) and then LDA to generate the aryne **16,** adduct **12l** was obtained in 25% yield. As Table 1 shows, similar results were obtained for amides **5m,n** under these conditions.

We also tried to apply the intramolecular Diels–Alder cycloaddition to the synthesis of lycorines with an expanded D ring (homolycorynes). When amide **18** (Scheme 5) was treated with LDA, the formation of three products was observed: tetracyclic compound **19** was isolated in only 4% yield, the major reaction products being compounds **21** and **22**, in yields which varied with reaction conditions. For short reaction times and at low temperature, quinoline derivative **21** was obtained as major product and **22** as minor; for longer reaction time and at higher temperature, the proportion of **22** increases. These products were probably formed as shown in Scheme 5. Intramolecular nucleophilic attack on the aryne gives phenyl carbanion intermediate **20**, which intramolecularly attacks the carbonyl group to give **22**.[10] DDQ oxidation of **22** afforded quinoline **23**.

Scheme 6



Finally, we studied the transformation of dihydroindoles **7**, **10**, **12**, and **13** into the corresponding indoles. Treatment of compounds **7**, **10**, **12**, and **13** with DDQ afforded the indole derivatives **7'**, **10'**, **12'**, and **13'** in good to excellent yields (Scheme 6). It may be possible to carry out the cycloaddition reaction and this type of oxidation in one pot by treatment of amides **5** with LDA or LTMP, followed by in situ oxidation with DDQ (see Table 1, conditions c).

Experimental Section

General Procedures. Solvents were dried by distillation from a drying agent:[11] THF, benzene, and DME from Na/benzophenone; $CHCl_3$, pyridine, CH_3CN, Et_3N, TMSCl, diisopropylamine, 2-methyl-2-propanol and HTMP from CaH_2; acetone from K_2CO_3; CH_2Cl_2 and DMF from P_2O_5. Melting

points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 250.13 and 62.83 MHz. LR and HR mass spectra were recorded at 70 eV or using FAB. Plate chromatography was performed on silica gel 60 F_{254} Merck or aluminum oxide 60 F_{254} (type E) Merck and visualized with UV light (254 and 360 nm), iodine vapors, ethanolic cerium–molybdenum, and *p*-anisaldehyde. Column chromatography (flash technique) on silica gel 60 (230–400 mesh ASTM) Merck or neutral aluminum oxide 90 (70–230 mesh ASTM) Merck, activity grade III (6% H_2O). PC Model 4.41 and Mopac 6.0 (AM1 MMOK vectors for amides MNDO vectors for enolates) were run on a Macintosh Centris 660_{AV}.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]benzamide (5a). Procedure a. (a) LDA in dry THF (0.231 M, 4.85 mL, 4.08 equiv) was added to a cooled (−78 °C) solution of amide **5a** (100 mg, 0.275 mmol) in dry THF (30 mL) under Ar using a syringe pump (2 mL/h). (b) The mixture was stirred at rt until TLC (Al_2O_3 plates) indicated that none of the starting material remained (8 h). H_2O was added to destroy the base excess, and the solution was concentrated in vacuo and extracted with CH_2Cl_2. The organic extracts were dried over anhydrous Na_2SO_4, filtered through Celite, and evaporated to a residue. (c) The residue was purified by flash chromatography on silica gel using 25% ethyl acetate/hexane as eluent. (d) The products were identified as 1,2-dimethoxy-4,5,7a,11a-tetrahydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**11a**, 29 mg, 37%) and 1,2-dimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12a**, 25 mg, 32%). Compound **11a**: ^1H NMR ($CDCl_3$) δ 6.75 (s, 1H), 6.17–6.14 (m, 2H), 6.05–5.98 (m, 1H), 5.51 (dd, 1H, J = 9.4 and 2.6 Hz), 4.27–3.90 (m, 3H), 3.87 (s, 3H), 3.84 (s, 3H), 3.24–3.08 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 167.0, 149.9, 146.2, 134.6, 127.8, 124.9, 125.0, 123.8, 123.3, 115.5, 109.2, 61.1, 56.7, 45.8, 38.5, 32.7, 27.6 ppm. Compound **12a**: pale yellow crystals; mp 195–196 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 9.00 (dd, 1H, J = 8.3 and 0.6 Hz), 8.57 (dd, 1H, J = 7.9 and 1.3 Hz), 7.75 (dt, 1H, J = 8.3 and 1.3 Hz), 7.59 (dt, 1H, J = 8.3 and 0.6 Hz), 7.03 (s, 1H), 4.46 (t, 2H, J = 8.3 Hz), 3.96 (s, 3H), 3.92 (s, 3H), 3.36 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 159.6, 149.6, 146.1, 134.7, 133.3, 132.2, 128.1, 127.8, 127.6, 126.7, 125.2, 111.6, 111.2, 60.0, 57.3, 46.6, 27.1 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]benzamide (5a). Procedure b (Oxidation with Air). (a) LDA in dry THF (0.28 M, 11 mL, 2.8 equiv) was added to a cooled (−60 °C) solution of **5a** (400 mg, 1.099 mmol) in dry THF (300 mL) under Ar using a syringe pump (3 mL/h). (b) The mixture was stirred at −40 °C until TLC indicated that none of the starting material remained. Methanol was added to the reaction mixture until it was decolorized, and then air was bubbled through it for 10 min. (c) Flash chromatography on silica gel, 75% ethyl acetate/hexane. (d) The product was identified as 1,2-dimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12a**, 280 mg, 91%).

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2,3-dimethoxybenzamide (5b). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in dry THF (0.30 M, 4 mL, 2.6 equiv) was added (1 mL/h) to **5b** (200 mg, 0.472 mmol) in THF (300 mL) at −40 °C. (b) Air, rt, 8 h. (c) Flash chromatography on silica gel, 75% ethyl acetate/hexane. (d) 1,2,8,9-Tetramethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12b**, 16 mg, 10%)- and 1,2,11-trimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**13b**, 88 mg, 60%). Compound **12b**: yellow crystals; mp 185–186 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.86 (d, 1H, J = 9.2 Hz), 7.36 (d, 1H, J = 9.2 Hz), 6.97 (s, 1H), 4.42 (t, 2H, J = 8.3 Hz), 4.00 (s, 3H), 3.98 (s, 3H), 3.91 (s, 6H) 3.32 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 158.2, 153.3, 150.4, 149.5, 145.4, 134.2, 128.1, 124.8, 123.0, 122.5, 116.8, 110.7, 110.6, 61.6, 59.9, 57.3, 56.4, 46.7, 27.0 ppm. Compound **13b**: yellow crystals; mp 129–131 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.11 (dd, 1H, J = 7.7 and 1.8 Hz), 7.52 (t, 1H, J = 7.7 Hz), 7.24 (dd, 1H, J = 7.7 and 1.8 Hz), 7.01 (s, 1H), 4.36 (t, 2H, J = 8.3 Hz), 3.99 (s, 3H), 3.88 (s, 3H), 3.67 (s, 3H), 3.32 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 159.5, 157.1, 150.2, 146.2, 134.7, 130.8, 129.9, 128.7, 123.4, 122.5, 119.9, 114.5, 111.1, 60.4, 57.1, 56.1, 46.1, 27.1 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2,3,4-trimethoxybenzamide (5c). Procedure a described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.27 M, 5.1 mL, 6.3 equiv) was added (1 mL/h) to **5c** (100 mg, 0.220 mmol) in dry THF (20 mL) at 0 °C. (b) 0 °C for 4 h. (c) Plate chromatography on silica gel; eluent, 3% CH_3OH/CH_2Cl_2. (d) *rel*-(7a*S*,11a*S*)-1,2,8,9-Tetramethoxy-4,5,7a,10,11,11a-hexahydro-7*H*-pyrrolo-[3,2,1-*de*]phenanthridine-7,10-dione (**10c**, 48 mg, 61%): white powder; mp 139–140 °C; ^1H NMR ($CDCl_3$) δ 6.75 (s, 1H), 4.15 (s, 3H), 4.25–3.98 (m, 2H) 3.87 (s, 3H), 3.92–3.82 (m, 1H), 3.84 (s, 3H), 3.73 (s, 3H), 3.63 (d, 1H, J = 5.6 Hz), 3.44–3.07 (m, 2H), 2.62–2.35 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 192.5, 162.9, 161.5, 150.0, 146.0, 138.0 134.1, 123.6, 115.5, 109.7, 61.2, 60.6, 59.0, 56.6, 46.1, 46.0, 40.3, 32.0, 28.0 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2,3,4-trimethoxybenzamide (5c). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.30 M, 3.0 mL, 2.7 equiv, 1 mL/h) was added to **5c** (150 mg, 0.330 mmol) in THF (65 mL) at −40 °C. (b) Air, rt, 8 h. (c) Flash chromatography on silica gel; eluent, 20% CH_2Cl_2/ethyl acetate. (d) 1,2,8,9,10-Pentamethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12c**, 84 mg, 69%) and 1,2,10,11-tetramethoxy-4,5-dihydro-7*H*-pyrrolo-[3,2,1-*de*]phenanthridin-7-one (**13c**, 11 mg, 10%). Compound **12c**: pale yellow crystals; mp 199–200 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.57 (s, 1H), 7.03 (s, 1H), 4.43 (t, 2H, J = 8.3 Hz), 4.03 (s, 3H), 4.01 (s, 3H), 3.99 (s, 3H), 3.95 (s, 3H), 3.93 (s, 3H), 3.34 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 157.9, 156.1, 155.2, 149.2, 145.3, 143.3, 134.8, 131.6, 125.1, 116.1, 111.5, 110.2, 104.7, 62.00, 61.2, 60.2, 57.3, 55.7, 46.6, 26.9 ppm. Compound **13c**: pale yellow crystals; mp 148–149 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.38 (d, 1H, J = 8.8 Hz), 7.23 (d, 1H, J = 8.8 Hz), 7.10 (s, 1H), 4.41 (t, 2H, J = 8.4 Hz), 4.03 (s, 3H), 3.94 (s, 3H), 3.74 (s, 3H), 3.72 (s, 3H), 3.37 (t, 2H, J = 8.4 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 159.6, 156.7, 150.2, 146.7, 135.1, 126.7, 124.5, 123.9, 122.4, 112.1, 111.9, 110.3, 61.1, 57.4, 56.2, 45.9, 27.2 ppm.

Cyclization of *N*-[2-(2-Bromo-3,4-dimethoxyphenyl)-ethyl]-4,5-dimethoxybenzamide (5d). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.31 M, 3.0 mL, 3.7 equiv) was added (1.5 mL/h) to **5d** (107 mg, 0.252 mmol) in THF (65 mL) at −60 °C. (b) Air, rt, 10 h. (c) Plate chromatography on silica gel; eluent 50% ethyl ether/CH_2Cl_2. (d) 1,2,9,10-Tetramethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12d**, 65 mg, 76%) and 1,2,10,11-tetramethoxy-4,5-dihydro-7*H*-pyrrolo-[3,2,1-*de*]phenanthridin-7-one (**13d** = **13c**, 9 mg, 10%). Compound **12d**: pale yellow powder; mp 225–226 °C; ^1H NMR ($CDCl_3$) δ 8.52 (s, 1H), 7.94 (s, 1H), 6.97 (s, 1H), 4.44 (t, 2H, J = 7.7 Hz), 4.04 (s, 6H), 3.95 (s, 3H), 3.91 (s, 3H), 3.34 (t, 2H, J = 7.7 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 159.1, 152.3, 149.3, 149.2, 144.9, 134.3, 127.7, 125.3, 121.9, 111.0, 110.5, 108.6, 107.7, 60.2, 57.2, 56.0, 55.8, 46.5, 27.2 ppm.

Cyclization of *N*-[2-(2-Chloro-4-methoxyphenyl)ethyl]-3,4-dimethoxybenzamide (5e). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.31 M, 2.5 mL, 1.9 equiv) was added (1.0 mL/h) to **5e** (150 mg, 0.429 mmol) in THF (50 mL) at −30 °C. (b) Air, rt, 8 h. (c) Flash chromatography on silica gel; eluent (1) 40% ethyl acetate/hexane, (2) 75% ethyl acetate/hexane. (d) Starting material **5e** (30 mg, 20%), 1-(3,4-dimethoxybenzoyl)-6-methoxy-2,3-dihydro-1*H*-indole (**7e**, 31 mg, 22%), 1,9,10-trimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12e**, 48 mg, 36%), and 1,10,11-trimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**13e**, 10 mg, 7%). Compound **12e**: pale yellow crystals; mp 220–222 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.47 (s, 1H), 7.92 (s, 1H), 7.13 (d, 1H, J = 8.1 Hz), 6.63 (d, 1H, J = 8.1 Hz), 4.44 (t, 2H, J = 8.2 Hz), 4.02 (s, 6H), 4.00 (s, 3H), 3.30 (t, 2H, J = 8.2 Hz) ppm ^{13}C

(10) In this case the molecular mechanics calculated distance between the aryl carbanion and carbonyl carbon is 2.96 Å, whereas for the five-ring analog it is 3.15 Å (PC Model).

(11) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1988.

NMR ($CDCl_3$) δ 159.8, 156.1, 152.1, 148.6, 140.8, 128.6, 123.1, 123.0, 121.2, 108.7, 108.4, 106.9, 104.7, 56.0, 55.7, 47.1, 26.3 ppm. Compound **7e**: white crystals; mp 116–117 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 7.16–7.13 (m, 2H), 7.05 (d, 1H, J = 8.2 Hz), 6.87 (d, 1H, J = 8.1 Hz), 6.55 (dd, 1H, J = 8.2 and 2.3 Hz), 4.11 (t, 2H, J = 8.2 Hz), 3.90 (s, 3H), 3.87 (s, 3H), 3.70 (bs, 3H), 3.01 (t, 2H, J = 8.2 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 168.6, 159.1, 150.9, 149.0, 143.9, 129.2, 124.8, 124.1, 120.4, 111.0, 110.6, 109.8, 103.1, 55.8, 55.2, 51.4, 27.2 ppm. Compound **13e**: white crystals; mp 131–132 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.31 (d, 1H, J = 8.7 Hz), 7.26 (d, 1H, J = 8.2 Hz), 7.19 (d, 1H, J = 8.7 Hz), 6.73 (d, 1H, J = 8.2 Hz), 4.41 (t, 2H, J = 8.4 Hz), 4.00 (s, 3H), 3.98 (s, 3H), 3.74 (s, 3H), 3.34 (t, 2H, J = 8.4 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 160.6, 156.8, 156.7, 146.3, 142.1, 126.7, 125.1, 124.2, 122.4, 121.9, 111.6, 108.0, 106.3, 60.6, 56.4, 56.1, 46.6, 26.6 ppm.

Cyclization of *N*-[2-(2-Chloro-4-methoxyphenyl)ethyl]-2,3,4-trimethoxybenzamide (5f). Procedure b described above for **5a** was followed, with the following modifications: a) LDA in THF (0.30 M, 5.0 mL, 2.8 equiv) was added (1.0 mL/h) to **5f** (200 mg, 0.526 mmol) in THF (120 mL) at −40 °C. (b) Air, rt, 8 h. (c) Flash chromatography on silica gel; eluent 50% ethyl acetate/CH_2Cl_2. (d) 1,8,9,10-Tetramethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12f**, 110 mg, 61%) and 1,10,11-trimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]-phenanthridin-7-one (**13f**, 28 mg, 17%). Compound **12f**: pale yellow crystals; mp 164–165 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.52 (s, 1H), 7.14 (d, 1H, J = 8.1 Hz), 6.61 (d, 1H, J = 8.1 Hz), 4.40 (t, 2H, J = 8.3 Hz), 4.01 (s, 3H), 4.00 (s, 6H), 3.96 (s, 3H), 3.25 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 158.4, 156.4, 155.9, 155.0, 142.6, 141.4, 132.4, 123.9, 122.7, 115.5, 106.2, 105.6, 104.6, 61.9, 61.2, 56.1, 55.6, 47.1, 26.0 ppm. Compound **13f**, identical to **13e**.

Cyclization of *N*-[2-(2-Chloro-4-methoxyphenyl)ethyl]-2,3,4-trimethoxybenzamide (5f). Procedure c (Oxidation with DDQ). (a) LDA in dry THF (0.25 M, 7.4 mL, 5.0 equiv) was added to a cooled (0 °C) solution of amide **5f** (140 mg, 0.368 mmol) in dry THF (70 mL) under Ar using a syringe pump (1.0 mL/h). (b) The mixture was stirred at rt until TLC indicated that none of the starting material remained. Methanol was added to the reaction mixture until it was decolorized, and then the solvent was evaporated in vacuo. The residue was dissolved in CH_2Cl_2, which was then evaporated; this operation was carried out three times. The residue was redissolved in CH_2Cl_2, DDQ (167 mg, 0.736 mmol) was added, and the mixture was stirred for 1 h at rt. The mixture was filtered through Celite, dried, and concentrated to a residue. (c) Flash chromatography on silica gel using (1) 25% ethyl acetate/hexane, (2) 50% ethyl acetate/hexane as eluents. (d) The products were identified as 1,8,9,10-tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12f'**, 56 mg, 45%), 1,8,9,-10-tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**13f'**, 12 mg, 11%), and 1-(2,3,4-trimethoxybenzoyl)-6-methoxy-1*H*-indole (**7f'**, 13 mg, 10%). Compound **12f'**: pale yellow crystals; mp 148–150 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.48 (s, 1H), 7.96 (d, 1H, J = 3.6 Hz), 7.58 (d, 1H, J = 8.4 Hz), 6.97 (d, 1H, J = 8.4 Hz), 6.74 (d, 1H, J = 3.6 Hz), 4.07 (s, 3H), 4.04 (s, 6H), 3.99 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 157.1, 156.6, 155.9, 142.6, 132.8, 132.3, 122.9, 112.5, 122.1, 114.5, 109.5, 107.9, 106.3, 105.4, 61.9, 61.3, 56.4, 55.7 ppm. Compound **13f'**: pale yellow crystals; mp 103–105 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.45 (d, 1H, J = 8.8 Hz), 7.92 (d, 1H, J = 3.6 Hz), 7.70 (d, 1H, J = 8.4 Hz), 7.21 (d, 1H, J = 8.8 Hz), 7.11 (d, 1H, J = 8.4 Hz), 6.83 (d, 1H, J = 3.6 Hz), 4.06 (s, 3H), 4.03 (s, 3H), 3.78 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.5, 157.9, 156.1, 146.5, 133.4, 127.4, 126.3, 123.8, 122.3, 121.8, 121.3, 111.4, 110.5, 110.2, 105.5, 60.7, 57.1, 56.1 ppm. Compound **7f'**: white crystals; mp 114–115 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.07 (bs, 1H), 7.43 (d, 1H, J = 8.7 Hz), 7.13 (d, 1H, J = 9.0 Hz), 7.00 (d, 1H, J = 3.8 Hz), 6.94 (m, 1H), 6.76 (d, 1H, J = 8.7 Hz), 6.48 (d, 1H, J = 3.8 Hz), 3.93 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 166.9, 158.2, 156.1, 151.6, 142.2, 136.7, 126.3, 124.6, 123.7, 122.6, 121.1, 113.2, 108.3, 107.2, 100.6, 61.8, 61.0, 56.1, 55.7 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5,6-trimethoxyphenyl)-ethyl]-2,3,4-trimethoxybenzamide (5g). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.31 M, 5.4 mL, 4.0 equiv) was added (1.0 mL/h) to **5g** (205 mg, 0.424 mmol) in THF (120 mL) at −30 °C. (b) Air, rt, 8 h. (c) Flash chromatography on silica gel; eluents (1) 50% ethyl acetate/hexane, (2) 75% ethyl acetate/hexane, (3) ethyl acetate. (d) 1,2,3,8,9,10-Hexamethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12g**, 73 mg, 43%) and 1,2,3,10,11-pentamethoxy-4,5-dihydro-7*H*-pyrrolo-[3,2,1-*de*]phenanthridin-7-one (**13g**, 17 mg, 11%). Compound **12g**: white crystals; mp 123–124 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.42 (s, 1H), 4.37 (t, J = 8.3 Hz, 2H), 4.02 (s, 3H), 4.00 (s, 3H), 3.97 (s, 6H), 3.94 (s, 3H), 3.88 (s, 3H), 3.39 (t, J = 8.3 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.2, 156.3, 155.1, 150.8, 150.4, 142.6, 142.0, 137.2, 132.0, 114.8, 114.4, 105.2, 103.6, 61.9, 61.3, 61.2, 60.5, 59.8, 55.7, 46.6, 25.1 ppm. Compound **13g**: white crystals; mp 114–115 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.26 (d, J = 8.8 Hz, 1H), 7.14 (d, J = 8.8 Hz, 1H), 4.32 (t, J = 8.4 Hz, 2H), 4.01 (s, 3H), 3.95 (s, 3H), 3.85 (s, 3H), 3.72 (s, 3H), 3.65 (s, 3H), 3.36 (t, J = 8.4 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.0, 156.7, 152.2, 151.0, 145.9, 142.5, 137.7, 127.1, 124.6, 121.6, 114.2, 111.5, 107.6, 105.0, 61.6, 60.9, 56.2, 46.1, 25.1 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2,4,5-trimethoxybenzamide (5h). Procedure a described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.25 M, 5.0 mL, 3.6 equiv) was added (2 mL/h) to **5h** (160 mg, 0.352 mmol) in THF (50 mL) at −45°C. (b) Rt overnight. (c) Flash chromatography on silica gel; eluent 20% CH_2Cl_2/ethyl acetate. (d) *rel*-(7a*S*,11*S*,11a*S*)-1,2,8,11-Tetramethoxy-4,5,7a,10,11,11a-hexahydro-7*H*-pyrrolo-[3,2,1-*de*]-phenanthridine-7,10-dione (**10h**, 54 mg, 43%) and 1,2,8,9-tetramethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**13h**, 16 mg, 13%). Compound **10h**: white foam; mp 197–198 °C; ^1H NMR ($CDCl_3$) δ 6.76 (s, 1H), 5.46 (s, 1H), 4.23–4.00 (m, 2H) 3.92 (dd, 1H, J = 5.3 and 11.9 Hz), 3.85 (s, 3H), 3.81 (s, 6H), 3.67 (d, 1H, J = 11.9 Hz), 3.50 (d, 1H, J = 5.3 Hz), 3.37 (s, 3H), 3.35–3.09 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 195.8, 173.1, 162.7, 150.1, 147.1, 133.7, 122.7, 113.7, 109.7, 102.1, 80.2, 60.8, 60.6, 56.4, 47.4, 46.0, 38.6, 27.9 ppm. Compound **13h**, identical to **12d**.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2,4,5-trimethoxybenzamide (5h). Procedure c described above for **5f** was followed, with the following modifications: (a) LDA in THF (0.28 M, 5.0 mL, 3.2 equiv) was added (2 mL/h) to **5h** (200 mg, 0.441 mmol) in THF (100 mL) at −50 °C. (b) DDQ (200 mg, 0.881 mmol), 2 h. (c) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. (d) 1,2,8,10,11-Pentamethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12h'**, 57 mg, 35%) and 1,2,9,10-tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**13h'**, 25 mg, 17%). Compound **12h'**: pale yellow powder; mp 159–161 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 7.92 (d, 1H, J = 3.4 Hz), 7.33 (s, 1H), 6.78 (s, 1H), 6.74 (d, 1H, J = 3.4 Hz), 4.07 (s, 3H), 4.05 (s, 3H), 3.98 (s, 3H), 3.76 (s, 3H), 3.66 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.5, 158.1, 156.8, 151.8, 147.5, 141.3, 129.3, 126.9, 122.4, 122.0, 109.5, 108.4, 107.2, 98.0, 61.7, 60.9, 57.4, 57.2, 56.2 ppm. Compound **13h'**: white crystals; mp 199–200 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.60 (s, 1H), 8.04 (s, 1H), 8.00 (d, 1H, J = 3.6 Hz), 7.33 (s, 1H), 6.80 (d, 1H, J = 3.6 Hz), 4.10 (s, 3H), 4.07 (s, 3H), 4.06 (s, 3H), 4.01 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 169.0, 162.6, 158.3, 153.6, 151.3, 149.4, 146.0, 128.8, 123.4, 123.1, 121.1, 110.3, 108.6, 106.6, 60.6, 57.0, 56.2, 56.0 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-3,4-(methylenedioxy)benzamide (5i). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.25 M, 7.8 mL, 8.0 equiv) was added (<1 mL/h) to **5i** (100 mg, 0.245 mmol) in THF (30 mL) at −40 °C and then rt overnight. (b) Air, 4 h. (c) Flash chromatography on silica gel; eluent 75% ethyl acetate/hexane. (d) 1,2-Dimethoxy-10,11-(methylenedioxy)-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**13i**, 30 mg, 38%): pale yellow powder; mp 217–219 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.26 (d, 1H, J = 8.4 Hz), 7.10 (d, 1H, J = 8.4 Hz), 7.04 (s, 1H), 6.18 (s, 2H), 4.39 (t, 2H, J = 8.4 Hz), 3.90 (s, 3H), 3.84 (s, 3H), 3.33 (t, 2H, J = 8.4 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 159.1, 151.3,

150.4, 145.8, 143.8, 134.8, 124.8, 124.3, 123.0, 116.2, 112.5, 109.0, 101.2, 61.7, 57.5, 46.3, 27.1 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-methoxy-3,4-(methylenedioxy)benzamide (5j). Procedure b described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.28 M, 6.0 mL, 4.5 equiv) was added (1 mL/h) to **5i** (164 mg, 0.374 mmol) in THF (120 mL) at −50 °C. (b) Air, rt, overnight. (c) Flash chromatography on silica gel; eluent (1) 50% ethyl acetate/hexane, (2) 75% ethyl acetate/hexane, (3) ethyl acetate. (d) 1,2,8-Trimethoxy-9,10-(methylenedioxy)-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12j**, 23 mg, 17%) and 1,2-dimethoxy-10,11-(methylenedioxy)-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]-phenanthridin-7-one (**13j**, 71 mg, 58%). Compound **12j**: mp 260−261 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.40 (s, 1H), 7.00 (s, 1H), 6.13 (s, 2H), 4.40 (t, 2H, J = 8.3 Hz), 4.9 (s, 3H), 3.90 (s, 6H), 3.32 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 158.1, 152.2, 149.2, 145.5, 144.5, 139.3, 134.6, 131.7, 124.9, 116.8, 111.4, 110.5, 102.1, 101.5, 61.4, 60.1, 57.4, 46.6, 29.6, 26.9 ppm. Compound **13j**, identical to **13i**.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-3,4-(methylenedioxy)-2-(trimethylsilyl)benzamide (5k). Procedure a described above for **5a** was followed, with the following modifications: (a) LDA in THF (0.29 M, 3.0 mL, 2.8 equiv) was added (0.5 mL/h) to **5k** (150 mg, 0.313 mmol) in THF (50 mL) at −40 °C. (b) Rt, overnight. (c) Flash chromatography on silica gel; eluent 30% ethyl acetate/hexane. (d) 5,6-Dimethoxy-1-[3,4-(methylenedioxy)-2-(trimethylsilyl)-benzoyl]-2,3-dihydro-1*H*-indole (**7k**, 59 mg, 47%) and **13k** (11 mg, 11%). Compound **7k**: white foam; ^1H NMR ($CDCl_3$, 60 °C) δ 6.84−6.73 (m, 3H), 5.94 (s, 2H), 4.26−3.36 (bs, 2H), 3.82 (s, 6H), 3.02 (t, 2H, J = 8.3 Hz), 0.25 (s, 9H) ppm. Compound **13k**, identical to **13i** and **13j**.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-hydroxy-3-methoxybenzamide (5l). Procedure d. A solution of LDA in THF (4 mL, 0.33 M, 3.6 equiv) was added dropwise to a solution of **5l** (150 mg, 0.367 mmol) in THF (50 mL) at −78 °C. $B(OMe)_3$ (50 mL, 0.440 mmol) was added, and the mixture was stirred for 15 min, treated with a solution of LDA in THF (0.5 mL, 0.9 equivs., 0.33 mM), and stirred at rt overnight. Methanol (1 mL) was added, and the mixture was acidified with diluted HCl and extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was dried over Na_2SO_4, and the solvent was evaporated. Flash chromatography on silica gel using 50% ethyl acetate/hexane as eluent afforded 1-(2-hydroxy-3-methoxybenzoyl)-5,6-dimethoxy-2,3-dihydro-1*H*-indole (**7l**, 60 mg, 50%) as white crystals: mp 144−145 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.60 (bs, 1H), 7.06−6.84 (m, 4H), 6.77 (s, 1H), 4.19 (t, 2H, J = 8.0 Hz), 3.93 (s, 3H), 3.87 (s, 6H), 3.07 (t, 2H, J = 8.0 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 167.6, 148.1, 146.4, 136.0, 123.7, 121.0, 119.9, 119.1, 113.3, 108.2, 102.7, 56.3, 56.1, 56.1, 51.2, 28.3 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-hydroxy-3-methoxybenzamide (5l). Procedure e. (a) Dichlorodiphenylsilane (70 μL, 0.337 mmol) was added to a stirred solution of **5l** (125 mg, 0.306 mmol) and Et_3N (95 μL, 0.672 mmol) in THF (50 mL) under Ar. (b) The white suspension formed was stirred for 1 h at rt and then cooled to −40 °C. LDA in dry THF (0.27 M, 6 mL, 5.3 equivs.) was added using a syringe pump (1 mL/h), and the mixture was stirred at rt overnight. Methanol (1 mL) was added to the reaction mixture, which was then acidified with diluted HCl and extracted with CH_2Cl_2 (3 × 50 mL). The organic extracts were dried over Na_2SO_4 and concentrated to a residue. (c) The residue was purified by flash chromatography on silica gel, using 40% ethyl acetate/hexane as eluent. (d) The products were identified as 8-hydroxy-1,2,9-trimethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12l**, 25 mg, 25%) and starting material **5l** (40 mg, 32%). Compound **12l** was crystallized from C_2H_5OH as yellow crystals: mp 223−224 °C; ^1H NMR ($CDCl_3$) δ 13.67 (s, 1H), 8.44 (d, 1H, J = 9.0 Hz), 7.30 (d, 1H, J = 9.0 Hz), 6.99 (s, 1H), 4.43 (t, 2H, J = 8.3 Hz), 4.00 (s, 3H), 3.93 (s, 6H), 3.38 (t, 2H, J = 8.3 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 163.6, 156.2, 154.4, 151.7, 150.5, 147.2, 133.0, 126.2, 125.1, 116.8, 116.7, 112.2, 110.3, 59.9, 57.1, 56.3, 46.1, 27.2 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-hydroxy-3,4-dimethoxybenzamide (5m). Procedure a described above for **5a** was followed, with the following modifications: (a) LTMP in THF (0.31 M, 4.6 mL, 4.0 equiv) was added (1.5 mL/h) to **5m** (160 mg, 0.364 mmol) in THF (65 mL) at −35 °C. (b) Rt, overnight. (c) Flash chromatography on silica gel; eluent 5% ethyl ether/CH_2Cl_2. Subsequently, plate chromatography on silica gel; eluent 5% ethyl ether/CH_2Cl_2. (d) 1-(2-Hydroxy-3,4-dimethoxybenzoyl)-5,6-dimethoxy-2,3-dihydro-1*H*-indole (**7m**, 66 mg, 51%) and 8-hydroxy-1,2,9,-10-tetramethoxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12m**, 25 mg, 20%). Compound **12m**: white powder; mp 168−170 °C (ethyl acetate); ^1H NMR ($CDCl_3$) δ 13.53 (bs, 1H), 8.06 (s, 1H), 6.95 (s, 1H), 4.34 (t, 2H, J = 7.9 Hz), 3.99 (s, 3H), 3.96 (s, 3H), 3.91 (s, 6H), 3.31 (t, 2H, J = 7.9 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 162.9, 156.9, 155.5, 150.0, 145.5, 135.8, 133.4, 130.0, 125.4, 111.5, 111.1, 107.3, 99.8, 60.6, 60.1, 57.1, 55.7, 46.0, 27.1 ppm. Compound **7m**: white crystals; mp 199−200 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 9.91 (s, 1H), 7.51 (bs, 1H), 7.21 (d, 1H, J = 8.9 Hz), 6.77 (s, 1H), 6.48 (d, 1H, J = 8.9 Hz), 4.24 (t, 2H, J = 7.9 Hz), 3.91 (s, 6H), 3.87 (s, 3H), 3.86 (s, 3H), 3.07 (t, 2H, J = 7.9 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 167.9, 155.0, 152.3, 147.4, 145.4, 136.3, 135.4, 123.1, 123.0, 112.7, 107.4, 101.9, 102.3, 60.0, 55.6, 55.4, 55.3, 51.5, 27.9 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-hydroxy-3,4-dimethoxybenzamide (5m). Procedure e described above for **5l** was followed, with the following modifications: (a) Dichlorodiphenylsilane (70 μL, 0.312 mmol) was added to a solution of **5m** (125 mg, 0.284 mmol) and Et_3N (90 μL, 0.625 mmol) in dry THF (50 mL) stirring at −78 °C. (b) 30 min at −40 °C. LTMP (0.35 M, 4.3 mL, 5.3 equiv) in dry THF (1 mL) was added (1 mL/h); rt overnight; CH_3OH (1 mL) then dilute HCl were added until acid; extracted with CH_2Cl_2 (3 × 25 mL). (c) Flash chromatography on silica gel; eluent 5% ethyl ether/CH_2Cl_2. (d) The products were identified as starting material **5m** (18 mg, 14%), **12m** (37 mg , 36%), and **7m** (18 mg, 18%).

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-hydroxy-3,4-(methylenedioxy)benzamide (5n). Procedure a described above for **5a** was followed, with the following modifications: (a) LTMP in THF (4.6 mL, 4.0 equivalents, 0.31 M) was added (1 mL/h) to **5n** (150 mg 0.354 mmol) in THF (60 mL) at −40 °C. (b) Rt, 5 h, and then CH_3-OH (1 mL) and HCl (until the solution was acidic) were added prior to extraction. (c) Flash chromatography on silica gel; eluent 3% ethyl ether/CH_2Cl_2. (d) 1-[2-Hydroxy-3,4-(methylenedioxy)benzoyl]-5,6-dimethoxy-2,3-dihydro-1*H*-indole (**7n**, 63 mg, 52%) and 8-hydroxy-1,2-dimethoxy-9,10-(methylene)dioxy-4,5-dihydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**12n**, 12 mg, 10%). Compound **7n**: white powder; mp 196−198 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 10.50 (bs, 1H), 7.47 (bs, 1H), 7.09 (d, 1H, J = 8.4 Hz), 6.78 (s, 1H), 6.43 (d, 1H, J = 8.4 Hz), 6.05 (s, 2H), 4.27 (t, 2H, J = 7.8 Hz), 3.87 (s, 3H), 3.86 (s, 3H), 3.07 (t, 2H, J = 7.8 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 169.0, 151.6, 148.1, 146.6, 144.8, 135.9, 135.1, 123.9, 123.1, 113.9, 108.1, 103.2, 102.2, 99.7, 56.3, 56.2, 53.0, 28.8 ppm. Compound **12n**: white powder; mp 222−224 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 13.53 (s, 1H), 7.97 (s, 1H), 6.96 (s, 1H), 6.12 (s, 2H), 4.36 (t, 2H, J = 8.2 Hz), 3.91 (s, 3H), 3.89 (s, 3H), 3.33 (t, 2H, J = 8.2 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 162.9, 152.9, 150.1, 145.4, 133.3, 133.0, 129.9, 125.3, 111.8, 110.9, 108.9, 102.3, 97.8, 60.1, 57.1, 46.1, 27.2 ppm.

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-ethyl]-2-hydroxy-3,4-(methylenedioxy)benzamide (5n). Procedure e described above for **5l** was followed, with the following modifications: (a) Dichlorodiphenylsilane (70 μL, 0.325 mmol) was added to a solution of **5n** (125 mg, 0.295 mmol) and Et_3N (90 μL, 0.620 mmol) in dry THF (50 mL) with stirring at −30 °C. (b) 1 h at rt, and then LDA (5 mL, 4.2 equiv, 0.25 M) was added (1.7 mL/h); 30 min at −30 °C; CH_3-OH (1 mL), then dilute HCl were added until acidic; extracted with CH_2Cl_2 (3 × 25 mL). (c) Flash chromatography on silica gel; eluent 40% ethyl acetate/hexane. (d) Compound **12n** (30 mg, 30%).

Cyclization of *N*-[2-(2-Bromo-4,5-dimethoxyphenyl)-propyl]-3,4-dimethoxybenzamide (18). Procedure a de-

scribed above for **5a** was followed, with the following modifications: (a) LDA in THF (0.34 M, 6 mL, 3.2 equivs) was added (2.0 mL/h) to **18** (280 mg, 0.639 mmol) in THF (70 mL) at −30 °C. (b) −30 °C, 1 h. (c) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. Subsequently, plate chromatography on silica gel; eluent 75% ethyl ether/hexane. (d) 1,2,10,12-Tetramethoxy-5,6-dihydro-4*H*,8*H*-pyrido[3,2,1-*de*]-phenanthridin-8-one (**19**, 8 mg, 4%), 1-(3,4-dimethoxybenzoyl)-6,7-dimethoxy-1,2,3,4-tetrahydroquinoline (**21**, 108 mg, 47%), and 8-(3,4-dimethoxybenzoyl)-6,7-dimethoxy-1,2,3,4-tetrahydroquinoline (**22**, 45 mg, 20%). Compound **19**: ^{1}H NMR ($CDCl_3$) δ 8.87 (s, 1H), 8.00 (s, 1H), 6.92 (s, 1H), 4.29 (t, 2H, *J* = 5.9 Hz), 4.05 (s, 6H), 3.94 (s, 3H), 3.88 (s, 3H), 2.99 (t, 2H, *J* = 6.2 Hz), 2.11 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 160.4, 152.5, 149.4, 147.8, 145.4, 129.1, 127.5, 120.9, 120.6, 114.3, 113.9, 108.8, 108.5, 60.2, 56.6, 56.0, 55.9, 42.7, 28.8, 20.8 ppm. Compound **21**: white crystals; mp 142−143 °C (ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 7.02 (d, 1H, *J* = 1.9 Hz), 6.88 (dd, 1H, *J* = 1.9 and 8.3 Hz), 6.69 (d, 1H, *J* = 8.3 Hz), 6.58 (s, 1H), 6.34 (bs, 1H), 3.85 (t, 2H, *J* = 6.2 Hz), 3.83 (s, 3H), 3.80 (s, 3H), 3.77 (s, 3H), 3.41 (s, 3H), 2.75 (t, 2H, *J* = 6.7 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 169.5, 150.6, 148.7, 146.5, 146.0, 132.2, 128.7, 122.5, 122.0, 112.0, 110.9, 110.2, 109.4, 55.9, 55.8, 55.6, 44.7, 26.3, 24.0 ppm. Compound **22**: yellow crystals; mp 119−120 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 7.53 (d, 1H, *J* = 1.9 Hz), 7.34 (dd, 1H, *J* = 1.9 and 8.4 Hz), 6.80 (d, 1H, *J* =8.4 Hz), 6.67 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.77 (s, 3H), 3.56 (s, 3H), 3.17 (t, 2H, *J* = 5.5 Hz), 2.72 (t, 2H, *J* = 6.4 Hz), 1.86 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$) δ 196.2, 153.2, 148.9, 146.2, 143.2, 137.7, 131.6, 125.4, 118.8, 117.6, 110.7, 109.9, 61.2, 57.1, 55.9, 41.5, 27.1, 21.6 ppm.

Oxidation with DDQ. General Procedure. (a) DDQ (1.2 equiv) was added to a stirred solution of the amide in dry CH_2Cl_2. When the reaction was complete (TLC, 0.5−1 h) the mixture was filtered through Celite, and the filtrates were evaporated in vacuo. (b) The residue was chromatographed on silica gel.

5,6-Dimethoxy-1-[3,4-(methylenedioxy)-2-(trimethylsilyl)benzoyl]-1*H*-indole (7k'). (a) DDQ (11 mg, 0.048 mmol) was reacted with **7k** (18 mg, 0.045 mmol) in CH_2Cl_2 (1 mL) for 30 min at rt. (b) Flash chromatography on silica gel; eluent 20% ethyl acetate/hexane. Compound **7k'** (17 mg, 95%): white foam; mp 55−56 °C; ^{1}H NMR ($CDCl_3$) δ 8.02 (bs, 1H), 7.02 (s, 1H), 6.95 (d, 1H, *J* = 3.6 Hz), 6.93 (d, 1H, *J* = 7.8 Hz), 6.85 (d, 1H, *J* = 7.8 Hz), 6.46 (d, 1H, *J* = 3.6 Hz), 6.02 (s, 2H), 3.98 (s, 3H), 3.94 (s, 3H), 0.17 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$) δ 169.8, 153.2, 148.2, 147.6, 147.3, 134.3, 130.2, 126.2, 123.7, 122.4, 118.8, 108.4, 102.5, 100.7, 100.4, 56.3, 56.1, −0.5 ppm.

1-(2-Hydroxy-3-methoxybenzoyl)-5,6-dimethoxy-1*H*-indole (7l'). (a) DDQ (22 mg, 0.098 mmol) was reacted with **7l** (27 mg, 0.082 mmol) in CH_2Cl_2 (2 mL) for 30 min. (b) Flash chromatography on silica gel; eluent 40% ethyl acetate/hexane. Compound **7l'** (18 mg, 67%): white powder, mp 108−109 °C; ^{1}H NMR ($CDCl_3$) δ 8.16 (s, 1H), 8.03 (s, 1H), 7.19 (d, 1H, *J* = 3.7 Hz), 7.13 (dd, 1H, *J* = 1.5 and 7.8 Hz), 7.06 (dd, 1H, *J* = 1.5 and 8.1 Hz), 7.03 (s, 1H), 6.94 (t, 1H, *J* = 8.0 Hz), 6.51 (d, 1H, *J* = 3.7 Hz), 3.98 (s, 3H), 3.95 (s, 3H), 3.94 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 168.4, 148.4, 148.1, 147.6, 147.4, 130.2, 126.3, 123.7, 121.8, 119.4, 114.6, 108.8, 102.8, 100.5, 56.2 ppm.

Oxidation of *rel*-(7a*S*,11a*R*)-1,2,8,9-Tetramethoxy-4,5,7a,10,11,11a-hexahydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridine-7,10-dione (10c). (a) **10c** (54 mg, 0.150 mmol) in CH_2Cl_2 (3 mL) was treated with DDQ (38 mg, 0.165 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. *rel*-(7a*S*,11a*S*)-1,2,8,9-Tetramethoxy-7a,10,11,11a-tetrahydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridine-7,10-dione (**10c'**, 45 mg, 84%) and 10-hydroxy-1,2,8,9-tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (**14**, traces). Compound **10c'**: white crystals; mp 163−164 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 7.58 (d, 1H, *J* = 3.6 Hz), 7.01 (s, 1H), 6.64 (d, 1H, *J* = 3.6 Hz), 4.19 (s, 3H), 4.11 (ddd, 1H, *J* = 5.8, 4.4 and 13.5 Hz), 3.94 (dd, 1H, *J* = 5.8 and 1.4 Hz), 3.92 (s, 3H), 3.91 (s, 3H), 3.76 (s, 3H), 2.71 (ddd, 1H, *J* = 4.4, 1.4 and 17.0 Hz), 2.43 (dd, 1H, *J* = 17.0 and 13.5 Hz) ppm; ^{13}C NMR ($CDCl_3$) δ 192.4, 163.5, 160.1, 151.4, 144.1, 138.6, 128.2, 123.5, 121.6, 114.9 110.7, 103.4 , 61.6, 60.8 , 59.7, 56.3, 48.1, 41.2, 32.5 ppm. Compound **14**: ^{1}H NMR ($CDCl_3$) δ 8.55 (s, 1H), 7.99 (d, 1H, *J* = 3.5 Hz), 7.31 (s, 1H), 6.76 (d, 1H, *J* = 3.5 Hz), 6.39 (bs, 1H), 4.10 (s, 3H), 4.03 (s, 3H), 4.01 (s, 3H), 3.99 (s, 3H) ppm.

Oxidation of *rel*-(7a*S*,11*S*,11a*S*)-1,2,8,11-Tetramethoxy-7a,10,11,11a-hexahydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridine-7,10-dione (10h). (a) **10h** (54 mg, 0.150 mmol) in CH_2Cl_2 (3 mL) was treated with DDQ (38 mg, 0.165 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. (d) *rel*-(7a*S*,11*S*,11a*S*)-1,2,8,11-Tetramethoxy-7a,10,11,11a-tetrahydro-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7,10-dione (**10h'**) (45 mg, 84%): white crystals; mp 207−208 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 7.58 (d, 1H, *J* = 3.6 Hz), 7.04 (s, 1H), 6.67 (d, 1H, *J* = 3.6 Hz), 5.56 (s, 1H), 4.16 (dd, 1H, *J* = 5.7 and 11.6 Hz), 3.94 (s, 3H), 3.92 (s, 3H), 3.89 (d, 1H, *J* = 5.7 Hz), 3.87 (s, 3H), 3.75 (d, 1H, *J* = 11.6 Hz), 3.33 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 191.5, 172.0, 163.0, 161.2, 151.6, 146.2, 122.9, 121.4, 113.0, 110.9, 103.8, 102.7, 81.2, 61.5, 60.8, 56.8, 56.4 , 48.7, 39.5 ppm.

1,2-Dimethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (12a'). (a) **12a** (135 mg, 0.480 mmol) in CH_2Cl_2 (10 mL) was treated with DDQ (120 mg, 0.528 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/CH_2Cl_2. Compound **12a'** (133 mg, 99%): yellow powder; mp 178−179 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 9.01 (dd, 1H, *J* = 8.2 and 1.0 Hz), 8.82 (dd, 1H, *J* = 8.2 and 2.0 Hz), 7.95 (d, 1H, *J* = 3.6 Hz), 7.79 (dt, 2H, *J* = 1.0 and 7.2 Hz), 7.59 (dt, 1H, *J* = 1.0 and 7.2 Hz), 7.28 (s, 1H), 6.77 (d, 1H, *J* = 3.6 Hz), 4.03 (s, 3H), 3.98 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.5, 151.3, 146.6, 133.8, 133.5, 129.4, 127.9, 127.1, 127.0, 126.2, 123.3, 122.7, 110.6, 110.1, 106.9, 60.5, 56.8 ppm.

1,2,8,9-Tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (12b'). (a) **12b** (67 mg, 0.196 mmol) in CH_2Cl_2 (10 mL) was treated with DDQ (54 mg, 0.236 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 10% THF/CH_2Cl_2. Compound **12b'** (57 mg, 86%): yellow powder; mp 155−156 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 8.86 (d, 1H, *J* = 9.1 Hz), 7.95 (d, 1H, *J* = 3.6 Hz), 7.38 (d, 1H, *J* = 9.1 Hz), 7.21 (s, 1H), 6.73 (d, 1H, *J* = 3.6 Hz), 4.02 (s, 3H), 3.97 (s, 3H), 3.96 (s, 3H), 3.95 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 156.7, 153.4, 152.0, 151.2, 145.6, 128.1, 125.7, 123.5, 122.9, 122.7, 121.5, 117.5, 110.1, 109.8, 105.6, 61.4, 60.2, 56.7, 56.2 ppm.

1,2,11-Trimethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (13b'). (a) **13b** (136 mg, 0.437 mmol) in CH_2Cl_2 (15 mL) was treated with DDQ (119 mg, 0.524 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent CH_2Cl_2. Compound **13b'** (112 mg, 82%): yellow powder; mp 110−111 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 8.28 (d, 1H, *J* = 7.7 Hz), 7.94 (d, 1H, *J* = 3.3 Hz), 7.60 (t, 1H, *J* = 8.0 Hz), 7.39−7.34 (m, 2H), 6.82 (d, 1H, *J* = 3.3 Hz), 4.07 (s, 3H), 3.99 (s, 3H), 3.79 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.3, 157.6, 152.4, 147.2, 129.4, 129.0, 126.6, 123.2, 122.6, 122.1, 121.8, 116.4, 111.1, 109.3, 106.8, 61.5, 57.0, 56.4 ppm.

1,2,8,9,10-Pentamethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (12c'). **12c** (35 mg, 0.094 mmol) in CH_2Cl_2 (3 mL) was treated with DDQ (26 mg, 0.113 mmol) for 30 min. (b) Flash chromatography on silica gel; eluent 40% ethyl acetate/hexane. Compound **12c'** (34 mg, 98%): yellow crystals; mp 131−132 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 8.63 (s, 1H,), 7.99 (d, 1H, *J* = 3.5 Hz, 7.31 (s, 1H), 6.75 (d, 1H, *J* = 3.5 Hz), 4.07 (s, 3H), 4.04 (s, 3H), 4.02 (s, 3H), 4.00 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 157.4, 157.0, 156.5, 151.1, 146.0, 143.4, 132.3, 126.1, 123.2, 123.2, 115.2, 109.7, 109.5, 106.8, 105.7, 61.9, 61.3, 60.4, 56.9, 55.9 ppm.

1,2,10,11-Tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (13c'). (a) **13c** (31 mg, 0.091 mmol) in CH_2Cl_2 (2 mL) was treated with DDQ (25 mg, 0.109 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 40% ethyl acetate/hexane. Compound **13c'** (20 mg, 65%): pale yellow crystals; mp 140−141 °C (C_2H_5OH); ^{1}H NMR ($CDCl_3$) δ 8.49 (d, 1H, *J* = 8.8 Hz), 7.95 (d, 1H, *J* = 3.5 Hz), 7.37 (s, 1H), 7.24 (d, 1H, *J* = 8.8 Hz), 6.81 (d, 1H, *J* = 3.5 Hz), 4.04 (s, 3H), 3.99 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.1, 152.2, 147.3, 147.2, 127.6, 126.8, 123.0, 122.1, 121.4, 111.9, 110.5, 109.7, 107.0, 62.2, 61.3, 57.0, 56.3 ppm.

1,9,10-Trimethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (12e'). (a) **12e** (45 mg, 0.145 mmol) in CH_2Cl_2 (2 mL)

was reacted with DDQ (72 mg, 0.318 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. Compound **12e'** (40 mg, 89%); yellow crystals; mp 183–184 °C (C_2H_5OH); ^1H NMR ($CDCl_3$) δ 8.42 (s, 1H), 7.98 (s, 1H), 7.95 (d, 1H, J = 3.6 Hz), 7.59 (d, 1H, J = 8.5 Hz), 6.98 (d, 1H, J = 8.5 Hz), 6.78 (d, 1H, J = 3.6 Hz), 4.08 (s, 3H), 4.05 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.3, 155.8, 153.2, 148.7, 132.2, 129.2, 122.5, 122.4, 122.3, 120.2, 110.2, 109.9, 109.2, 107.9, 105.9, 56.2, 56.0, 55.8 ppm.

1,2,9,10-Tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (13h'). (a) **13h** (= **12d**, 15 mg, 0.044 mmol) in CH_2Cl_2 (2 mL) was reacted with DDQ (15 mg, 0.066 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. Compound **13h'** (14 mg, 94%): pale yellow crystals; mp 199–200 °C (C_2H_5OH).

1,2-Dimethoxy-10,11-(methylenedioxy)-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (13i'). (a) **13i** (107 mg, 0.329 mmol) in CH_2Cl_2 (5 mL) was treated with DDQ (82 mg, 0.362 mmol) for 3 h. (b) Flash chromatography on silica gel; eluent 50% CH_2Cl_2/hexane. Compound **13i'** (90 mg, 85%): yellow powder; mp 203–204 °C (CH_3OH); ^1H NMR ($CDCl_3$) δ 8.36 (d, 1H, J = 8.4 Hz), 7.95 (d, 1H, J = 3.6 Hz), 7.94 (s, 1H), 7.10 (d, 1H, J = 8.4 Hz), 6.79 (d, 1H, J = 3.6 Hz), 6.24 (s, 2H), 3.97 (s, 3H), 3.92 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$) δ 158.0, 152.6, 152.2, 146.3, 144.4, 126.5, 123.5, 122.4, 122.1, 116.3, 110.5, 108.8, 107.6, 101.5, 62.4, 57.0 ppm.

1,2,8-Trimethoxy-9,10-(methylenedioxy)-7*H*-pyrrolo-[3,2,1-*de*]phenanthridin-7-one (12j'). (a) **12j** (18 mg, 0.051 mmol) in CH_2Cl_2 (3 mL) was treated with DDQ (14 mg, 0.061 mmol) for 1 h. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/hexane. Compound **12j'** (14 mg, 78%): yellow powder; mp 215–216 °C; ^1H NMR ($CDCl_3$) δ 8.44 (s, 1H), 7.97 (d, 1H, J = 3.6 Hz), 7.30 (s, 1H), 6.74 (d, 1H, J = 3.6 Hz), 6.16 (s, 2H), 4.14 (s, 3H), 3.99 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 156.6, 153.3, 151.1, 146.2, 146.1, 139.1, 132.5, 125.7, 123.0, 115.6, 109.8, 109.6, 106.7, 102.4, 102.3, 61.3, 60.5, 56.9 ppm.

8-(3,4-Dimethoxybenzoyl)-6,7-dimethoxyquinoline (23). (a) **22** (33 mg, 0.093 mmol) in CH_2Cl_2 (2 mL) was treated with DDQ (51 mg, 0.223 mmol) for 30 min. (b) Flash chromatography on silica gel; eluent 50% ethyl acetate/CH_2Cl_2. Compound **23** (32 mg, 97%): white powder; mp 216–217 °C; ^1H NMR ($CDCl_3$) δ 8.66 (dd, 1H, J = 1.7 and 4.3 Hz), 8.03 (dd, 1H, J = 1.7 and 8.3 Hz), 7.77 (d, 1H, J = 2.0 Hz), 7.27 (dd, 1H, J = 4.3 and 8.3 Hz), 7.15 (dd, 2H, J = 2.0 and 8.3 Hz), 6.73 (d, 1H, J = 8.3 Hz), 4.03 (s, 3H), 3.94 (s, 3H), 3.87 (s, 6H) ppm; ^{13}C NMR ($CDCl_3$) δ 194.6, 153.8, 152.3, 149.3, 148.8, 148.7, 143.0, 134.2, 131.3, 126.0, 125.9, 110.5, 120.6, 110.1, 106.8, 61.8, 55.9 ppm.

Methylation of 10-Hydroxy-1,2,8,9-tetramethoxy-7*H*-pyrrolo[3,2,1-*de*]phenanthridin-7-one (14). MeI (2 drops) was added to a suspension of **14** (5 mg, 0.014 mmol) and K_2CO_3 (3 mg, 0.021 mmol) in acetone (2 mL), and the mixture was refluxed for 1 h. The solvent was evaporated, and the residue was dissolved in CH_2Cl_2 and washed with water. The organic phase was dried over Na_2SO_4, filtered, and concentrated to a residue. This product was identical to **12c'**.

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Supporting Information Available: Experimental procedure for the synthesis of amides **5a–n**, **18**, and their precursors, copies of spectra (^1H and ^{13}C NMR) and further spectroscopic and analytical data for compounds **5**, **7**, **10–13**, **18**, **19**, and **21–23**, and results of MNDO calculations for coefficients at C_2 and C_6 on model compounds (85 pages). This material is contained in libraries on microfiche, inmediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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