[Chem. Pharm. Bull.]
32(8)2984—2994(1984)

**Studies on the Chemical Constituents of Rutaceous Plants. LV.¹⁾ The Development of a Versatile Method for the Synthesis of Antitumor-Active Benzo[*c*]phenanthridine Alkaloids. (5).¹⁾
A New Method for Quaternization of the Benzo[*c*]phenanthridine Nucleus**

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(Received November 18, 1983)

A versatile method of synthesis of the quaternary benzo[*c*]phenanthridine alkaloid (1), having a tertiary benzo[*c*]phenanthridine skeleton, from the norbase (3) is described.

Treatment of the norbase (3) with sodium borohydride in formic or in acetic acid gave the *N*-methyl- (5) or the *N*-ethyl- (7) dihydrobase, respectively, in good yield. The *N*-methyldihydrobase (5) could also be prepared by treatment of the norbase (3) with sodium borohydride and dimethyl sulfate in hexamethylphosphoric triamide. The dihydrobases (5 and 7) were readily convertible to the corresponding quaternary benzo[*c*]phenanthridine alkaloids by oxidation with Jones reagent or with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in good yields.

In addition, we found that the air-oxidation of the carbanions derived from the ψ -cyanides (11) of the quaternary bases (1) gave the corresponding oxybases (10) in excellent yields.

Keywords—quaternary benzo[*c*]phenanthridine alkaloid synthesis; *N*-alkyl-5,6-dihydrobenzo[*c*]phenanthridine; tertiary benzo[*c*]phenanthridine; *N*-alkylbenzo[*c*]phenanthridone; air-oxidation of ψ -cyanide carbanion; sodium borohydride–acetic acid; sodium borohydride–formic acid; sodium borohydride–dimethyl sulfate in hexamethylphosphoric triamide

It is well known that the quaternary bases of fully aromatized benzo[*c*]phenanthridine alkaloids²⁾ (1) occur naturally in Rutaceous plants, especially *Xanthoxylum* species. Among them, nitidine³⁾ (1a) and fagaronine⁴⁾ (2) are important because of strong antitumor activity against various types of experimental tumors (L1210, P388, S180A, *etc.*). These findings stimulated us to develop a preparative method for these alkaloids. Several synthetic sequences^{4b,5)} have been reported and some of them involve a direct quaternization step^{3b,4b,5a)} of a tertiary benzo[*c*]phenanthridine nucleus (the norbases) (3) with dimethyl sulfate in a mixed solvent of xylene and nitrobenzene at the last stage in the reaction sequences. Although this procedure was used as a general method for the quaternization of the norbases (3), Stermitz^{4b)} reported the formation of an inseparable mixture of the salt (1) of the desired quaternary base and the protic salt (4) of the starting norbase when this procedure was applied to the synthesis of fagaronine (2). Apart from their description,^{4b)} we have also experienced this problem, that is, when the norbases (3) were treated even with “magic methyl” (FSO₃CH₃), an inseparable mixture of almost equal amounts of the salts of quaternary and tertiary bases. Therefore, an improved method for the quaternization of the norbase (3) is desirable in the chemistry of benzo[*c*]phenanthridine alkaloids. In this report, we describe the establishment of a general procedure for this purpose.

Onda^{5b,c)} reported that dehydrogenation of *N*-methyl-5,6-dihydrobenzo[*c*]phenanthri-

Chart 1

dine derivatives (the NMe-dihydrobases) (**5**) with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) provided the quaternary bases (**1**) in good yields. Therefore, we undertook to transform compounds having a tertiary benzo[*c*]phenanthridine skeleton [the norbases (**3**)] into the NMe-dihydrobases (**5**). As starting materials for our studies, two norbases (**3a** and **3b**) were prepared from naturally occurring benzo[*c*]phenanthridinium alkaloids [nitidine (**1a**) and chelerythrine (**1b**)] by thermal decomposition. Initially, we aimed at converting the norbases (**3**) into the NH-5,6-dihydrobenzo[*c*]phenanthridine derivatives (the NH-dihydrobases) (**6**), because Eschweiler–Clarke reaction⁶⁾ of the resulting NH-dihydrobases (**6**) would be expected to give the desired NMe-dihydrobases (**5**) in good yields. Actually, however, treatment of norchelerythrine (**3b**) with sodium borohydride in acetic acid gave an unexpected product (**7b**), almost quantitatively. The ultraviolet (UV) spectrum of the product (**7b**) was superimposable on that of dihydrochelerythrine⁷⁾ (**5b**). In the proton nuclear magnetic resonance (¹H-NMR) spectrum, it shows a 2H quartet ($J = 7.0$ Hz) at δ 2.78 coupled with a 3H triplet ($J = 7.0$ Hz) at δ 1.20, indicating the presence of an *N*-ethyl group in the molecule. These results led us to assign the product as *N*-ethyl-5,6-dihydronorchelerythrine (**7b**). Since *N*-alkylation of NH-compounds with sodium borohydride in carboxylic acids had already been reported,⁸⁾ this conclusion is reasonable. General applicability of this method for reductive *N*-ethylation of the norbases was confirmed by the preparation of three other *N*-ethyldihydrobases (**7a**, **7d**, and **7e**) from the corresponding norbases (**3a**, **3d**, and **3e**) (Table I).

This finding provided a hint for a direct preparative method for the NMe-dihydrobases (**5**) from the norbases (**3**). Treatment of norchelerythrine (**3b**) and *O*-ethyldecarine^{5d)} (**3d**) with sodium borohydride in formic acid produced the desired dihydrochelerythrine (**5b**) and *N*-methyl-5,6-dihydro-*O*-ethyldecarine (**5d**) in good yields, respectively. This method seems to have potential applicability to a phenolic norbase. This view is supported by the finding that treatment of decarine^{5d, 9)} (**3f**), a naturally occurring phenolic base, with sodium borohydride in formic acid gave the desired *N*-methyl-5,6-dihydrodecarine (**5f**) in 79.3% yield. This

TABLE I. Yields of the Dihydrobases (5 or 7) from the Norbases (3)

No. of norbase (3)	Substituents			7		5	
	R ₁	R ₂	R ₃	NaBH ₄ in AcOH (%)	NaBH ₄ in HCO ₂ H (%)	NaBH ₄ with Me ₂ SO ₄ (%)	
a	H	OMe	OMe	62.4	—	79.7	
b	OMe	OMe	H	85.2	88.8	80.3	
c	H	OCH ₂ O		—	—	77.7	
d	OMe	OEt	H	88.3	76.1	—	
e	OEt	OMe	H	96.6	—	79.4	
f ^{a)}	OMe	OH	H	—	79.7	—	
g	OMe	OMe	OMe	—	—	84.1	

a) A naturally occurring base²⁾: decarine.

dihydrobase (5f) was used for structural establishment of the new quaternary phenolic base isolated from *Macleaya cordata* (WILLD.) R. Br. [*Bocconia cordata* WILLD.] (Papaveraceae: Japanese name "Takenigusa" or "Champagiku") by Takao *et al.*¹⁰⁾

The above procedure is versatile in small-scale experiments but has the defect that a large amount of sodium borohydride is consumed. We, therefore, attempted to develop another procedure which is suitable for large-scale operation. When treated with an alkylating reagent, the norbase (3) was transformed into a mixture of the *N*-methylated quaternary salt (1) and the protic salt (4) of the starting norbase as stated above. Then, subsequent treatment of the reaction mixture with sodium borohydride resulted in formation of a mixture of the desired *N*-methylated dihydrobase (5) produced from the former salt (1) and the starting norbase (3) recovered from the latter one (4). Thus, taking into account the fact that dialkyl sulfate does not undergo reduction with sodium borohydride, when an adequate amount of the alkylating reagent is present in the reaction mixture, the recovered norbases (3) should be converted into a mixture of the *N*-methylated quaternary salt (1) and the protic salt (4) again. This consideration led us to conclude that such a pathway should operate when the norbases (3) are treated with an excess amount of sodium borohydride in the presence of an adequate amount of an alkylating reagent in a suitable solvent. In other words, we anticipated that the cyclic pathway would finally provide only the desired *N*-methylated dihydrobase (5) in good yield. In fact, treatment of a mixture of norchelerythrine (3b) and dimethyl sulfate in hexamethylphosphoric triamide (HMPA) with sodium borohydride afforded dihydrochelerythrine (5b) almost quantitatively. It should be noted here that similar treatment of the same norchelerythrine (3b) with diethyl sulfate, instead of dimethyl sulfate, resulted in recovery of the starting material (3b). This result reflects the difference of reactivity between these two

alkylating reagents in an S_N2 type reaction. Five NMe-dihydrobases (**5**) were prepared from the corresponding norbases (**3**) by this procedure (Table I).

It is well known that separation of a mixture of quaternary benzo[*c*]phenanthridine alkaloids (**1**) is very difficult, so that, sometimes, the natural occurrence of these alkaloids has to be verified as the dihydrobases (**5**) after reduction of the crude mixture with sodium borohydride. As described above, in the course of transformation of α -allocryptopine (**8**) and protopine (**9**) into chelerythrine (**1b**) and sanguinarine (**1h**), Onda *et al.*^{5b)} succeeded in the dehydrogenation of dihydrochelerythrine (**5b**) and dihydrosanguinarine (**5h**) with DDQ to provide the corresponding quaternary bases (**1b** and **1h**) in good yields. Therefore, our seven dihydrobases (**5** and **7**) were converted to the desired quaternary bases (**1**) as shown in Table II according to their method.^{5b,c)} On the other hand, in the course of studies on oxidation of the dihydrobases (**5**) for another purpose, we occasionally found that oxidation with Jones reagent is also applicable to this conversion. This reagent was applied to nine dihydrobases¹¹⁾ and gave the corresponding quaternary bases in fairly good yields as shown in Table II. Onda's method gave excellent results, but our method has the advantages of simple operation

TABLE II. Yields of the Quaternary Bases (**1**) from the Dihydrobases (**5** or **7**) and of the Oxybases (**10**) from the Quaternary Bases (**1**) by Various Methods

Substituents				No. of the dihydrobase	Yield of the quaternary base (1) chloride			Yield of the oxybase (10)		
R	R ₁	R ₂	R ₃		No.	With DDQ (%)	With Jones reagent (%)	No.	With K ₃ Fe(CN) ₆ (%)	via the ψ -cyanide (11) (%)
Me	H	OMe	OMe	5a	a ^{a)}	—	92.3	a	76.3 ¹⁸⁾	58.5
Me	OMe	OMe	H	5b	b ^{a)}	—	79.7	b	—	61.9
Me	H	OCH ₂ O		5c	c ^{a)}	—	81.7	c	—	56.9
Me	OMe	OEt	H	5d	d	67.5	—	d	34.3	—
Me	OEt	OMe	H	5e	e	87.2	78.3	e	—	69.3
Me	OMe	OMe	OMe	5g	g	87.5	85.4	g	—	—
Me	OCH ₂ O		H	5h	h ^{a)}	54.9 ^{b)}	85.4	h	—	59.7
Et	H	OMe	OMe	7a	i	83.0	—	i	48.1	—
Et	OMe	OMe	H	7b	j	85.6	93.2	j	45.8	—
Et	OMe	OEt	H	7d	k	64.9	72.0	k	28.9	61.8
Et	OEt	OMe	H	7e	l	—	79.4	l	—	56.5

a) A naturally occurring base²⁾: **a** (nitidine), **b** (chelerythrine), **c** (avicine), **h** (sanguinarine).

b) As the sulfate.

and a cheaper reagent.

Since, generally speaking, the quaternary bases (**1**) tended to bear undefined contents of water of crystallization, the derived quaternary bases were characterized as the oxybases (**10**) and/or the ψ -cyanides (**11**). In 1937, Späth¹²⁾ oxidized sanguinarine (**1h**) to oxysanguinarine (**10h**) by treatment with potassium ferricyanide in aqueous potassium hydroxide solution. This procedure is now a general method for this transformation. Therefore, five quaternary bases were derived to the corresponding oxybases (**10**) according to the general method. However, this method usually provided the desired oxybases in unsatisfactory yields. In the course of studies aimed at the preparation of a carbanion of the ψ -cyanide (**11**) of the quaternary bases, we occasionally found that the carbanion readily underwent air-oxidation to the corresponding oxybase (**10**) in good yield. We applied this method to seven quaternary bases (**1**) and obtained the corresponding oxybases (**10**) in fairly good yields. All of the oxybases¹³⁾ described in this report provided reasonable elemental analyses and spectral data, as described in Experimental. In conclusion, one of several restrictive steps in the Robinson synthetic sequence^{5a,e,f)} for benzo[*c*]phenanthridine alkaloids has been by-passed by the establishment of our general method for the preparation of the quaternary bases (**1**) from the norbases (**3**).

Experimental

Instruments, etc., were as described in the preceding paper.^{1b)}

Nornitidine (3a)—Nitidine (**1a**) chloride (0.244 g) was heated at 110 °C for 10 h under reduced pressure (1 mmHg). Recrystallization of the residue from CHCl₃–MeOH gave yellow needles (0.152 g), mp 280–282 °C. *Anal.* Calcd for C₂₀H₁₅NO₄: C, 72.06; H, 4.54; N, 4.20. Found: C, 71.93; H, 4.46; N, 4.16. ¹H-NMR (CF₃CO₂H) δ : 4.23 and 4.37 (each 3H, s, OCH₃), 6.23 (2H, s, OCH₂O), 7.41 and 7.76 (each 1H, s, C₁– and C₇–H), 7.99 and 8.16 (each 1H, s, arom. H), 8.11 and 8.42 (each 1H, d, *J* = 8.0 Hz, C₁₂– and C₁₁–H), 9.33¹⁴⁾ (1H, d, *J* = 8.0 Hz, C₆–H).

General Procedure for Reductive *N*-Alkylation of the Norbases (3**) with Sodium Borohydride in Acetic or Formic Acid [*N*-Alkyl-5,6-dihydrobenzo[*c*]phenanthridine Derivatives (The *N*-Alkyldihydrobases) (**5** or **7**)]**—Sodium borohydride (100–200 mol) was added portionwise to a stirred solution of the norbase (**3**) (1 mol) in AcOH or HCO₂H at room temperature. The reaction proceeded exothermically with foaming. After being stirred at room temperature for 30 min, the reaction mixture was made weakly alkaline with 10% NaOH aq. and extracted with CHCl₃ or ethyl acetate. The organic layer was dried over K₂CO₃ and evaporated to dryness. The residue was purified by column chromatography on Al₂O₃ (neutral, grade III) with benzene, followed by recrystallization from a suitable solvent to give the desired *N*-alkyldihydrobase (**5** or **7**).

5-Ethyl-8,9-dimethoxy-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*N*-Ethyl-5,6-dihydronornitidine) (7a**)**—Nornitidine (**3a**) (0.180 g), AcOH (20 ml), and NaBH₄ (3.00 g) gave colorless prisms (0.123 g), mp 174–177 °C (benzene–MeOH). *Anal.* Calcd for C₂₂H₂₁NO₄: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.77; H, 5.90; N, 3.80. ¹H-NMR δ : 1.16 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 2.78 (2H, q, *J* = 7.0 Hz, NCH₂CH₃), 3.92 and 3.96 (each 3H, s, OCH₃), 4.15 (2H, s, ArCH₂N), 5.99 (2H, s, OCH₂O), 6.75, 7.08, 7.28, and 7.60 (each 1H, s, C₇–, C₁–, C₁₀–, and C₄–H), 7.45 and 7.67 (each 1H, d, *J* = 8.5 Hz, C₁₂– and C₁₁–H).

5-Ethyl-7,8-dimethoxy-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*N*-Ethyl-5,6-dihydronorchelerythrine) (7b**)**—Norchelerythrine¹⁵⁾ (**3b**) (0.093 g), AcOH (8 ml), and NaBH₄ (1.70 g) gave colorless fine needles (0.086 g), mp 147–148 °C (benzene–MeOH). *Anal.* Calcd for C₂₂H₂₁NO₄: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.77; H, 5.84; N, 3.83. ¹H-NMR δ : 1.20 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 2.78 (2H, q, *J* = 7.0 Hz, NCH₂CH₃), 3.89 and 3.92 (each 3H, s, OCH₃), 4.34 (2H, s, ArCH₂N), 6.02 (2H, s, OCH₂O), 6.91 and 7.69 (each 1H, d, *J* = 8.5 Hz, C₉– and C₁₁–H), 7.45 and 7.49 (each 1H, d, *J* = 8.5 Hz, arom. H), 7.10 and 7.63 (each 1H, s, C₁– and C₄–H).

8-Ethoxy-5-ethyl-7-methoxy-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*N,O*-Diethyl-5,6-dihydrodecarine) (7d**)**—*O*-Ethyldecarine^{5d)} (**3d**) (0.157 g), AcOH (20 ml), and NaBH₄ (1.70 g) gave colorless prisms (0.150 g), mp 162–164.5 °C (benzene–MeOH). *Anal.* Calcd for C₂₃H₂₃NO₄ · 1/4CH₃OH: C, 72.45; H, 6.27; N, 3.63. Found: C, 72.24; H, 6.01; N, 3.62. ¹H-NMR δ : 1.19 and 1.49 (each 3H, t, *J* = 7.0 Hz, CH₂CH₃), 2.78 (2H, q, *J* = 7.0 Hz, NCH₂CH₃), 3.91 (3H, s, OCH₃), 4.14 (2H, q, *J* = 7.0 Hz, OCH₂CH₃), 4.34 (2H, s, ArCH₂N), 6.02 (2H, s, OCH₂O), 6.90 and 7.69 (each 1H, d, *J* = 8.5 Hz, C₉– and C₁₁–H), 7.09 and 7.62 (each 1H, s, C₁– and C₄–H), 7.45 (2H, d, *J* = 8.5 Hz, C₁₀– and C₁₂–H).

7-Ethoxy-5-ethyl-8-methoxy-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*N,O*-Diethyl-5,6-dihydroisodecarine) (7e**)**—*O*-Ethylisodecarine^{5d)} (**3e**) (0.298 g), AcOH (30 ml), and NaBH₄ (3.27 g) gave colorless prisms (0.313 g), mp 195–200 °C (CHCl₃–MeOH). *Anal.* Calcd for C₂₃H₂₃NO₄: C, 73.19; H, 6.14; N, 3.71. Found: C,

72.82; H, 6.10; N, 3.57. $^1\text{H-NMR}$ δ : 1.17 and 1.41 (each 3H, t, $J=7.0$ Hz, CH_2CH_3), 2.76 (2H, q, $J=7.0$ Hz, NCH_2CH_3), 3.87 (3H, s, OCH_3), 4.06 (2H, q, $J=7.0$ Hz, OCH_2CH_3), 4.32 (2H, s, ArCH_2N), 5.98 (2H, s, OCH_2O), 6.86 and 7.65 (each 1H, d, $J=9.3$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{11}\text{-H}$), 7.41 and 7.44 (each 1H, d, $J=9.3$ Hz, arom. H), 7.06 and 7.58 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$).

7,8-Dimethoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (Dihydrochelerythrine) (5b)—Norchelerythrine¹⁵⁾ (**3b**) (0.017 g), HCO_2H (2 ml), and NaBH_4 (0.189 g) gave colorless prisms (0.016 g), mp 166—168 °C ($\text{CHCl}_3\text{-MeOH}$) (lit.^{9b)} mp 167—170 °C).

8-Ethoxy-7-methoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*O*-Ethyl-*N*-methyl-5,6-dihydrodecarine) (5d)—*O*-Ethyldecarine^{5d)} (**3d**) (0.054 g), HCO_2H (6 ml), and NaBH_4 (0.760 g) gave colorless prisms (0.043 g), mp 167—171 °C (benzene— MeOH). *Anal.* Calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.90; H, 5.82; N, 3.78. $^1\text{H-NMR}$ δ : 1.48 (3H, t, $J=7.5$ Hz, CH_2CH_3), 2.57 (3H, s, NCH_3), 3.87 (3H, s, OCH_3), 4.13 (2H, q, $J=7.5$ Hz, OCH_2CH_3), 4.27 (2H, s, ArCH_2N), 5.99 (2H, s, OCH_2O), 6.88 and 7.66 (each 1H, d, $J=8.5$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{11}\text{-H}$), 7.06 and 7.64 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$), 7.44 (2H, d, $J=8.5$ Hz, $\text{C}_{10}\text{-}$ and $\text{C}_{12}\text{-H}$).

8-Hydroxy-7-methoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*N*-Methyl-5,6-dihydrodecarine) (5f)—Decarine⁹⁾ (**3f**) (0.024 g), HCO_2H (3 ml), and NaBH_4 (0.281 g) gave colorless plates (0.020 g), mp 169—173 °C (EtOH). *Anal.* Calcd for $\text{C}_{20}\text{H}_{17}\text{NO}_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.47; H, 5.14; N, 3.92. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3430 (OH), $^1\text{H-NMR}$ δ : 2.57 (3H, s, NCH_3), 3.84 (3H, s, OCH_3), 4.26 (2H, s, ArCH_2N), 5.64 (1H, s, OH), 6.01 (2H, s, OCH_2O), 6.97 and 7.68 (each 1H, d, $J=8.5$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{11}\text{-H}$), 7.09 and 7.65 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$), 7.47 (2H, d, $J=8.5$ Hz, $\text{C}_{10}\text{-}$ and $\text{C}_{12}\text{-H}$).

General Procedure for Reductive *N*-Alkylation of the Norbases (3) with Dimethyl Sulfate and Sodium Borohydride in Hexamethylphosphoric Triamide [The *N*-Methyldihydrobases (5)]—Sodium borohydride (5—15 mol) was added to a solution of the norbase (**3**) (1 mol) and dimethyl sulfate (18—35 mol) in HMPA at room temperature with stirring. The reaction mixture was heated at 50—60 °C (bath temperature). After 1 h, additional amounts of dimethyl sulfate (18—40 mol) and NaBH_4 (5—15 mol) were added. Then, the reaction mixture was heated at the same temperature for 0.5—1 h. The reaction mixture was made weakly basic with 5% NaOH aq. and extracted with ethyl acetate. The ethyl acetate solution was washed with water and sat. NaCl aq., dried over K_2CO_3 , and evaporated to dryness. The residue was purified by column chromatography on Al_2O_3 (basic, grade II) with benzene or by preparative TLC on SiO_2 followed by recrystallization from a suitable solvent to give the desired *N*-methyldihydrobase (**5**).

8,9-Dimethoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (Dihydranitidine) (5a)—Noranitidine (**3a**) (0.102 g), Me_2SO_4 (0.5 ml), HMPA (5 ml), and NaBH_4 (0.060 g) were used. Additional Me_2SO_4 (1.5 ml) and NaBH_4 (0.180 g) were required. Colorless prisms (0.086 g), mp 220—224 °C ($\text{CHCl}_3\text{-MeOH}$) (lit.¹⁶⁾ mp 223.5—224 °C).

7,8-Dimethoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (Dihydrochelerythrine) (5b)—Norchelerythrine¹⁵⁾ (**3b**) (0.050 g), Me_2SO_4 (0.5 ml), HMPA (3 ml), and NaBH_4 (0.085 g) were used. Additional Me_2SO_4 (0.5 ml) and NaBH_4 (0.085 g) were required. Colorless prisms (0.042 g), mp 167—169 °C (benzene— MeOH) (lit.^{9b)} mp 167—170 °C).

5-Methyl-2,3,8,9-bismethylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (Dihydroavicine) (5c)—Noravicine^{1b)} (**3c**) (0.032 g), Me_2SO_4 (0.19 ml), HMPA (2 ml), and NaBH_4 (0.057 g) were used. Additional Me_2SO_4 (0.38 ml) and NaBH_4 (0.113 g) were required. Colorless prisms (0.026 g), mp 217—219 °C ($\text{CHCl}_3\text{-MeOH}$) (lit.¹⁶⁾ mp 223—224 °C).

7-Ethoxy-8-methoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (*O*-Ethyl-*N*-methyl-5,6-dihydroisodecarine) (5e)—*O*-Ethylisodecarine^{5d)} (**3e**) (0.104 g), Me_2SO_4 (0.5 ml), HMPA (3 ml), and NaBH_4 (0.056 g) were used. Additional Me_2SO_4 (0.5 ml) and NaBH_4 (0.056 g) were required. Colorless prisms (0.086 g), mp 198—205 °C (softened at 180—183 °C) (acetone). *Anal.* Calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.88; H, 5.84; N, 3.74. $^1\text{H-NMR}$ δ : 1.40 (3H, t, $J=7.5$ Hz, CH_2CH_3), 2.56 (3H, s, NCH_3), 3.87 (3H, s, OCH_3), 4.06 (2H, q, $J=7.5$ Hz, OCH_2CH_3), 4.27 (2H, s, ArCH_2N), 5.97 (2H, s, OCH_2O), 6.87 and 7.65 (each 1H, d, $J=8.5$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{11}\text{-H}$), 7.41 and 7.44 (each 1H, d, $J=8.5$ Hz, arom. H), 7.06 and 7.62 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$).

7,8,9-Trimethoxy-5-methyl-2,3-methylenedioxy-5,6-dihydrobenzo[*c*]phenanthridine (5g)—The norbase^{1b)} (**3g**) (0.525 g), Me_2SO_4 (2.7 ml), HMPA (15 ml), and NaBH_4 (0.263 g) were used. Additional Me_2SO_4 (5.3 ml) and NaBH_4 (0.256 g) were required. Pale yellow prisms (0.461 g), mp 163—165 °C ($\text{CHCl}_3\text{-MeOH}$). *Anal.* Calcd for $\text{C}_{22}\text{H}_{21}\text{NO}_5$: C, 69.64; H, 5.58; N, 3.69. Found: C, 69.63; H, 5.61; N, 3.63. $^1\text{H-NMR}$ δ : 2.56 (3H, s, NCH_3), 3.88, 3.89, and 3.93 (each 3H, s, OCH_3), 4.18 (2H, s, ArCH_2N), 6.00 (2H, s, OCH_2O), 7.04 (2H, s, $\text{C}_1\text{-}$ and $\text{C}_{10}\text{-H}$), 7.44 and 7.61 (each 1H, d, $J=9.0$ Hz, $\text{C}_{12}\text{-}$ and $\text{C}_{11}\text{-H}$), 7.62 (1H, s, $\text{C}_4\text{-H}$).

General Method^{5b,c)} for Oxidative Quaternization of the *N*-Alkyldihydrobases (5 or 7) with DDQ [*N*-Alkybenzo[*c*]phenanthridinium (1) Salts]—A solution of DDQ (1.5—3 mol) in benzene was added dropwise to a stirred solution of the *N*-alkyldihydrobase (**5** or **7**) (1 mol) in benzene containing dil. NaOH aq. at room temperature. The reaction mixture was stirred at room temperature for several hours, then the solvent was distilled off under reduced pressure. The residue was diluted with water and extracted with CHCl_3 . The chloroform solution was dried over K_2CO_3 and concentrated to ca. 1 ml. A large excess of 10% HCl aq. was dropped into the chloroform solution under ice-cooling. The resulting precipitates were collected by filtration and recrystallized from a suitable solvent to

give the desired quaternary base (1) salt.

8-Ethoxy-7-methoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (*O*-Ethyl-*N*-methyldecarinium) (1d) Chloride—DDQ (0.068 g) in benzene (2 ml) was added to *O*-ethyl-*N*-methyl-5,6-dihydrodecarine (5d) (0.035 g) in benzene (2 ml) and 5% NaOH aq. (1 ml). The reaction time was 1 h. Yellow needles (0.026 g), mp 189–192 °C (dec.) (H₂O); ¹H-NMR¹⁷⁾ (CF₃CO₂H) δ: 1.64 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 4.44 (3H, s, OCH₃), 4.48 (2H, q, *J* = 7.0 Hz, OCH₂CH₃), 5.06 (3H, s, N⁺CH₃), 6.24 (2H, s, OCH₂O), 7.52 and 8.04 (each 1H, s, C₁– and C₄–H), 8.12 and 8.21 (each 1H, d, *J* = 8.5 Hz, C₉– and C₁₂–H), 8.56 and 8.60 (each 1H, d, *J* = 8.5 Hz, arom. H), 9.78 (1H, s, C₆–H).

7-Ethoxy-8-methoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (*O*-Ethyl-*N*-methylisodecarinium) (1e) Chloride—DDQ (0.095 g) in benzene (2 ml) was added to *O*-ethyl-*N*-methyl-5,6-dihydroisodecarine (5e) (0.099 g) in benzene (8 ml) and 5% NaOH aq. (1 ml). The reaction time was 0.5 h. Yellow fine needles (0.095 g), mp 181–185 °C (dec.) (MeOH–isoPrOH). This material was identical with the sample prepared by oxidation with Jones reagent described below.

7,8,9-Trimethoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (1g) Chloride—DDQ (0.302 g) in benzene (12 ml) was added to the trimethoxy-dihydrobase (5g) (0.333 g) in benzene (15 ml) and 5% NaOH aq. (6.2 ml). The reaction time was 2 h. Pale yellow needles (0.318 g), mp 225–232 °C (softened at 190–195 °C) (dec.) (EtOH–MeOH). This material was identical with the sample prepared by oxidation with Jones reagent described below.

5-Methyl-2,3,7,8-bismethylenedioxybenzo[*c*]phenanthridinium (Sanguinarine) (1h) Sulfate—DDQ (0.136 g) in benzene (6 ml) was added to dihydrosanguinarine¹¹⁾ (5h) (0.103 g) in benzene (4 ml) and 10% NaOH aq. (2 ml). Salt formation was carried out using 10% H₂SO₄ aq. instead of 10% HCl aq. The reaction time was 2 h. Orange fine needles (0.073 g), mp > 300 °C (MeOH). This material was identical with the sample prepared by oxidation with Jones reagent described below.

5-Ethyl-8,9-dimethoxy-2,3-methylenedioxybenzo[*c*]phenanthridinium (*N*-Ethyl-*N*-nornitidine) (1i) Chloride—DDQ (0.103 g) in benzene (6 ml) was added to the dihydrobase (7a) (0.055 g) in benzene (3 ml) and 5% NaOH aq. (4 ml). The reaction time was 1 h. Yellow needles (0.050 g), mp 269–272 °C (dec.) (H₂O). ¹H-NMR (CF₃CO₂H) δ: 2.03 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 4.25 and 4.37 (each 3H, s, OCH₃), 5.33 (2H, q, *J* = 7.0 Hz, N⁺CH₂CH₃), 6.25 (2H, s, OCH₂O), 7.54 and 7.77 (each 1H, s, C₁– and C₇–H), 7.92 and 8.22 (each 1H, s, arom. H), 8.18 and 8.54 (each 1H, d, *J* = 8.5 Hz, C₁₂– and C₁₁–H), 9.41 (1H, s, C₆–H).

5-Ethyl-7,8-dimethoxy-2,3-methylenedioxybenzo[*c*]phenanthridinium (*N*-Ethyl-*N*-norchelerythrine) (1j) Chloride—DDQ (0.055 g) in benzene (4 ml) was added to the dihydrobase (7b) (0.035 g) in benzene (2 ml) and 5% NaOH aq. (1 ml). The reaction time was 1 h. Yellow needles (0.033 g), mp 160–164 °C (dec.) (dil. HCl aq.). This material was identical with the sample prepared by oxidation with Jones reagent described below.

8-Ethoxy-5-ethyl-7-methoxy-2,3-methylenedioxybenzo[*c*]phenanthridinium (*N,O*-Diethyldecarinium) (1k) Chloride—DDQ (0.100 g) in benzene (5 ml) was added to the dihydrobase (7d) (0.069 g) in benzene (4 ml) and 5% NaOH aq. (2 ml). The reaction time was 2 h. Yellow fine needles (0.049 g), mp 174–178 °C (dec.) (MeOH–acetone). This material was identical with the sample prepared by oxidation with Jones reagent described below.

General Procedure for Oxidative Quaternization of the *N*-Alkyldihydrobases (5 or 7) with Jones Reagent [*N*-Alkylbenzo[*c*]phenanthridinium (1) Chloride]—Jones reagent¹⁸⁾ (1.1–1.5 mol) was added to an ice-cooled solution of the *N*-alkyldihydrobase (5 or 7) (1 mol) in acetone with stirring. The reaction mixture was stirred at the same temperature for 30 min, basified with 10% NaOH aq., and extracted with CHCl₃. The chloroform solution was dried over K₂CO₃ and evaporated to dryness. The residue was dissolved in a small amount of CHCl₃ or CHCl₃–MeOH. Dilute HCl aq. was added dropwise to the solution under ice-cooling. The resulting precipitates were collected by filtration and recrystallized from a suitable solvent.

8,9-Dimethoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (Nitidine) (1a) Chloride—Dihydro-nitidine (5a) (0.074 g), acetone (15 ml), and Jones reagent (0.18 ml) gave yellow needles (0.075 g), mp 286–292 °C (dec.) (H₂O). (lit.^{9a)} mp 278–283 °C).

7,8-Dimethoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (Chelerythrine) (1b) Chloride—Dihydrochelerythrine (5b) (0.500 g), acetone (50 ml), and Jones reagent (0.87 ml) gave yellow prisms (0.438 g), mp 192–193 °C (dec.) (MeOH–acetone) (lit.^{9b)} mp 203–206 °C).

5-Methyl-2,3,8,9-bismethylenedioxybenzo[*c*]phenanthridinium (Avicine) (1c) Chloride—Dihydroavicine (5c) (0.100 g), acetone (20 ml), and Jones reagent (0.18 ml) gave yellow prisms (0.090 g), mp > 300 °C (MeOH). *Anal.* Calcd for C₂₀H₁₄ClNO₄·2H₂O: C, 59.48; H, 4.49; N, 3.47. Found: C, 59.64; H, 4.18; N, 3.52. ¹H-NMR (CF₃CO₂H) δ: 4.96 (3H, s, N⁺CH₃), 6.24 and 6.38 (each 2H, s, OCH₂O), 7.52 and 7.59 (each 1H, s, C₁– and C₇–H), 8.06 and 8.14 (each 1H, s, arom. H), 8.16 and 8.44 (each 1H, d, *J* = 9.0 Hz, C₁₂– and C₁₁–H), 9.21 (1H, s, C₆–H).

7-Ethoxy-8-methoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (*O*-Ethyl-*N*-methylisodecarinium) (1e) Chloride—The dihydrobase (5e) (0.220 g), acetone (20 ml), and Jones reagent (0.34 ml) gave yellow fine needles (0.188 g), mp 179–187 °C (dec.) (isoPrOH–MeOH). *Anal.* Calcd for C₂₂H₂₀ClNO₄·1/2H₂O: C, 64.97; H, 5.20; N, 3.44. Found: C, 64.80; H, 4.99; N, 3.38. ¹H-NMR (CF₃CO₂H) δ: 1.60 (3H, dif. t, *J* = 7.0 Hz, CH₂CH₃), 4.20 (3H, s, OCH₃), 4.70 (2H, dif. q, *J* = 7.0 Hz, OCH₂CH₃), 5.04 (3H, s, N⁺CH₃), 6.22 (2H, s, OCH₂O), 7.48 (1H, s, C₁–H), 7.90–8.36 (3H, m, arom. H × 3), 8.36–8.74 (2H, m, arom. H × 2), 9.76 (1H, s, C₆–H).

7,8,9-Trimethoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridinium (1g) Chloride—The trimethoxy-dihydrobase (**5g**) (0.061 g), acetone (5 ml), and Jones reagent (0.14 ml) gave yellow needles (0.057 g), mp 225–232 °C (dec.) (EtOH–MeOH). ¹H-NMR (CD₃OD) δ: 4.02, 4.27, and 4.35 (each 3H, s, OCH₃), 4.88 (3H, s, N⁺CH₃), 6.22 (2H, s, OCH₂O), 7.44 (1H, s, C₁–H), 7.93 (1H, dif. s, arom. H), 8.05 (2H, dif. s, arom. H × 2), 8.48–8.72 (1H, m, arom. H), 9.64 (1H, s, C₆–H).

5-Methyl-2,3,7,8-bismethylenedioxybenzo[*c*]phenanthridinium (Sanguinarine) (1h) Chloride—Dihydro-sanguinarine¹¹ (**5h**) (1.042 g), acetone (100 ml), and Jones reagent (1.88 ml) gave orange fine needles (0.982 g), mp 285–287 °C (dec.) (isoPrOH–MeOH) (lit.^{5c}) mp 286–288 °C).

5-Ethyl-7,8-Dimethoxy-2,3-methylenedioxybenzo[*c*]phenanthridinium (N-Ethyl-N-norchelerythrine) (1j) Chloride—The dihydrobase (**7b**) (0.019 g), acetone (0.4 ml), and Jones reagent (0.04 ml) gave yellow prisms (0.020 g), mp 160–164 °C (dec.) (isoPrOH–MeOH). ¹H-NMR¹⁷ (CF₃CO₂H) δ: 2.01 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 4.22 and 4.42 (each 3H, s, OCH₃), 5.38 (2H, dif. q, *J* = 7.0 Hz, N⁺CH₂CH₃), 6.24 (2H, s, OCH₂O), 7.52 and 7.90 (each 1H, s, C₁– and C₄–H), 8.14 and 8.22 (each 1H, d, *J* = 8.5 Hz, C₉– and C₁₂–H), 8.54 and 8.63 (each 1H, d, *J* = 8.5 Hz, arom. H), 9.84 (1H, s, C₆–H).

8-Ethoxy-5-ethyl-7-methoxy-2,3-methylenedioxybenzo[*c*]phenanthridinium (N,O-Diethyldecarinium) (1k) Chloride—The dihydrobase (**7d**) (0.150 g), acetone (15 ml), and Jones reagent (0.24 ml) gave yellow fine needles (0.118 g), mp 174–177 °C (dec.) (MeOH–acetone). ¹H-NMR (CD₃OD) δ: 1.56 and 1.80 (each 3H, t, *J* = 7.0 Hz, CH₂CH₃), 4.34 (3H, s, OCH₃), 4.41 (2H, m, OCH₂CH₃), 5.37 (2H, q, *J* = 7.0 Hz, N⁺CH₂CH₃), 6.26 (2H, s, OCH₂O), 7.51 and 7.94 (each 1H, s, C₁– and C₄–H), 8.16 and 8.58 (each 2H, d, *J* = 9.0 Hz, C₉–, C₁₂–, C₁₀–, and C₁₁–H), 9.97 (1H, s, C₆–H).

7-Ethoxy-5-ethyl-8-methoxy-2,3-methylenedioxybenzo[*c*]phenanthridinium (N,O-Diethylisodecarinium) (1l) Chloride—The dihydrobase (**7e**) (0.273 g), acetone (50 ml), and Jones reagent (0.6 ml) gave yellow prisms (0.237 g), mp 164–167 °C (dec.) (isoPrOH–MeOH). *Anal.* Calcd for C₂₃H₂₂ClNO₄ · 1/2H₂O: C, 65.63; H, 5.51; N, 3.33. Found: C, 65.38; H, 5.29; N, 3.34. ¹H-NMR¹⁷ (CF₃CO₂H) δ: 1.62 and 2.01 (each 3H, t, *J* = 7.0 Hz, CH₂CH₃), 4.21 (3H, s, OCH₃), 4.71 (2H, q, *J* = 7.0 Hz, OCH₂CH₃), 5.38 (2H, q, *J* = 7.0 Hz, N⁺CH₂CH₃), 6.24 (2H, s, OCH₂O), 7.51 and 7.87 (each 1H, s, C₁– and C₄–H), 8.14, 8.19, 8.55, and 8.60 (each 1H, d, *J* = 9.5 Hz, arom. H), 9.83 (1H, s, C₆–H).

General Procedure for Syntheses of 5-Alkylbenzo[*c*]phenanthridin-6(5H)-ones (The Oxybases) (10) by Oxidation of the Quaternary Base (1) Salts with Potassium Ferricyanide—The quaternary base (1) salt (1 mol) was dissolved in a solution of KOH (*ca.* 25 mol) in aqueous THF. An aqueous solution of K₃Fe(CN)₆ (5.5–10 mol) was dropped into the above solution with stirring under reflux. Refluxing was continued for several hours, then the reaction mixture was extracted with benzene or CHCl₃. The organic layer was dried over K₂CO₃ and evaporated to dryness *in vacuo*. Purification of the residue by preparative thin layer chromatography (p-TLC) followed by recrystallization from a suitable solvent gave the desired oxybase (10).

8-Ethoxy-7-methoxy-5-methyl-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5H)-one (10d)—K₃Fe(CN)₆ (0.200 g) in H₂O (4 ml) was added to the quaternary base (**1d**) chloride (0.033 g) in THF (5 ml), H₂O (10 ml), and KOH (0.103 g). The reaction time was 0.5 h. Colorless fine needles (0.011 g), mp 209–211 °C (benzene–MeOH). *Anal.* Calcd for C₂₂H₁₉NO₅: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.84; H, 5.07; N, 3.72. IR ν_{max}^{KBr} cm^{–1}: 1650 (CO). ¹H-NMR δ: 1.49 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 3.88 (3H, s, OCH₃), 4.10 (3H, s, NCH₃), 4.21 (2H, q, *J* = 7.0 Hz, OCH₂CH₃), 6.02 (2H, s, OCH₂O), 7.12 and 7.52 (each 1H, s, C₁– and C₄–H), 7.35 and 7.48 (each 1H, d, *J* = 8.5 Hz, C₉– and C₁₂–H), 7.93 and 7.94 (each 1H, d, *J* = 8.5 Hz, arom. H).

5-Ethyl-8,9-dimethoxy-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5H)-one (10i)—K₃Fe(CN)₆ (0.202 g) in H₂O (4 ml) was added to the quaternary base (**1i**) chloride (0.022 g) in THF (4 ml), H₂O (8 ml), and KOH (0.112 g). The reaction time was 0.5 h. Colorless prisms (0.010 g), mp 222–223.5 °C (benzene–MeOH). *Anal.* Calcd for C₂₂H₁₉NO₅: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.78; H, 5.02; N, 3.55. IR ν_{max}^{KBr} cm^{–1}: 1634 (CO). ¹H-NMR δ: 1.52 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 4.05 and 4.09 (each 3H, s, OCH₃), 4.51 (2H, q, *J* = 7.0 Hz, NCH₂CH₃), 6.07 (2H, s, OCH₂O), 7.13 and 7.89 (each 1H, s, C₁– and C₇–H), 7.50 and 7.92 (each 1H, d, *J* = 8.5 Hz, C₁₂– and C₁₁–H), 7.53 and 7.55 (each 1H, s, arom. H).

5-Ethyl-7,8-Dimethoxy-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5H)-one (10j)—K₃Fe(CN)₆ (0.203 g) in H₂O (4 ml) was added to the quaternary base (**1j**) chloride (0.040 g) in THF (10 ml), H₂O (12 ml), and KOH (0.098 g). The reaction time was 0.5 h. Colorless prisms (0.018 g), mp 185–188 °C (benzene–MeOH). *Anal.* Calcd for C₂₂H₁₉NO₅: C, 70.02; H, 5.07; N, 3.71. Found: C, 70.24; H, 5.03; N, 3.75. IR ν_{max}^{KBr} cm^{–1}: 1642 (CO). ¹H-NMR δ: 1.46 (3H, t, *J* = 7.0 Hz, CH₂CH₃), 3.96 and 4.08 (each 3H, s, OCH₃), 4.43 (2H, q, *J* = 7.0 Hz, NCH₂CH₃), 6.04 (2H, s, OCH₂O), 7.11 and 7.46 (each 1H, s, C₁– and C₄–H), 7.33 and 7.90 (each 1H, d, *J* = 9.0 Hz, C₉– and C₁₀–H), 7.47 and 7.92 (each 1H, d, *J* = 8.5 Hz, C₁₂– and C₁₁–H).

8-Ethoxy-5-ethyl-7-methoxy-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5H)-one (10k)—K₃Fe(CN)₆ (0.329 g) in H₂O (5 ml) was added to the quaternary base (**1k**) chloride (0.043 g) in THF (5 ml), H₂O (10 ml), and KOH (0.212 g). The reaction time was 3.5 h. Colorless fine needles (0.012 g), mp 177–179 °C (CHCl₃–MeOH). This material was identical with the sample prepared by air-oxidation of the ψ-cyanide (**11k**).

General Procedure for Syntheses of the Oxybases (10) by Air-Oxidation of the Carbanions Prepared from 5-Alkyl-6-cyano-5,6-dihydrobenzo[*c*]phenanthridine (The ψ-Cyanides) (11)—i) The ψ-Cyanides (**11**): Potassium cyanide

(1—2 mol) was added to a stirred solution of the quaternary base (1) salt (1 mol) in H₂O or aqueous MeOH at room temperature. Stirring was continued at room temperature or at 50—60 °C, if required, for *ca.* 1 h. The resulting precipitates were collected by filtration, then recrystallized from a suitable solvent to give the desired ψ -cyanide (11).

ii) The Oxybases (10) from the ψ -Cyanides (11): Sodium hydride¹⁹⁾ (1.5—3 mol) was added to a stirred solution of the ψ -cyanide (11) (1 mol) in HMPA at room temperature. The reaction mixture was stirred at room temperature for several hours. After addition of sat. NaCl aq., the reaction mixture was extracted with ethyl acetate. The organic layer was washed with sat. NaCl aq. several times, dried over K₂CO₃, and evaporated to dryness *in vacuo*. Recrystallization of the residue from a suitable solvent gave the desired oxybase (10).

8,9-Dimethoxy-5-methyl-2,3-methylenedioxybenzo[c]phenanthridin-6(5H)-one (Oxynitidine) (10a)—i) Nitidine ψ -Cyanide (11a): Nitidine (1a) chloride (0.209 g), H₂O (50 ml), and KCN (0.041 g) were heated for 0.5 h. Colorless prisms (0.140 g), mp 223—230 °C (softened at 210 °C) (CHCl₃–MeOH) [lit.²⁰⁾ mp 234 °C (softened at 215—216 °C)]. *Anal.* Calcd for C₂₂H₁₈N₂O₄: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.58; H, 4.80; N, 7.20. ¹H-NMR δ : 2.58 (3H, s, NCH₃), 3.92 and 3.96 (each 3H, s, OCH₃), 5.06 (1H, s, ArCHN), 6.02 (2H, s, OCH₂O), 6.92 and 7.08 (each 1H, s, arom. H), 7.30 and 7.62 (each 1H, s, C₁₀– and C₄–H), 7.51 and 7.63 (each 1H, d, *J*=9.0 Hz, C₁₂– and C₁₁–H).

ii) Oxynitidine (10a): Nitidine ψ -cyanide (11a) (0.095 g), HMPA (3.0 ml), and NaH (0.034 g) were used. The reaction time was 1 h. Colorless prisms (0.078 g), mp 286—288 °C (CHCl₃–MeOH) (lit.¹⁶⁾ mp 285—286 °C).

This material was identical with an authentic sample of oxynitidine.¹⁶⁾

7,8-Dimethoxy-5-methyl-2,3-methylenedioxybenzo[c]phenanthridin-6(5H)-one (Oxychelerythrine) (10b)—i) Chelerythrine ψ -Cyanide (11b): Chelerythrine (1b) chloride (0.514 g), H₂O (15 ml), and KCN (0.098 g) were heated for 1 h. Colorless prisms (0.371 g), mp 226—231 °C (acetone) (lit. mp 240—245 °C¹⁶⁾; mp 229—233 °C²¹⁾; mp 260—261 °C²²⁾). This material was identical with an authentic sample¹⁶⁾ of chelerythrine ψ -cyanide (11b).

ii) Oxychelerythrine (10b): The ψ -cyanide (11b) (0.046 g), HMPA (2 ml), and NaH (0.008 g) were used. The reaction time was 3.5 h. Colorless fine needles (0.037 g), mp 199—203 °C (CHCl₃–MeOH) (lit.^{9b)} mp 200—203 °C). This material was identical with an authentic sample of oxychelerythrine.^{9b)}

5-Methyl-2,3,8,9-bismethylenedioxybenzo[c]phenanthridin-6(5H)-one (Oxyavicine) (10c)—i) Avicine ψ -Cyanide (11c): Avicine (1c) sulfate²³⁾ (0.043 g), aqueous MeOH [MeOH (5 ml) and H₂O (15 ml)], and KCN (0.010 g) were heated for 0.5 h. Colorless prisms (0.026 g), mp > 300 °C (softened at 220 °C) (CHCl₃–MeOH) (lit.²⁴⁾ mp > 340 °C). *Anal.* Calcd for C₂₁H₁₄N₂O₄: C, 70.38; H, 3.94; N, 7.82. Found: C, 69.90; H, 3.94; N, 7.32. ¹H-NMR (DMSO-*d*₆) δ : 2.52 (3H, s, NCH₃), 5.68 (1H, s, ArCHN), 6.06 and 6.09 (each 2H, s, OCH₂O), 7.09, 7.30, 7.47, and 7.55 (each 1H, s, arom. H), 7.59 and 7.80 (each 1H, d, *J*=8.0 Hz, C₁₂– and C₁₁–H).

ii) Oxyavicine (10c): Avicine ψ -cyanide (11c) (0.060 g), HMPA (2.0 ml), and NaH (0.012 g) were used. The reaction time was 4.5 h. Colorless prisms (0.046 g), mp 281.5—282 °C (softened at 263—264 °C) (CHCl₃–EtOH) (lit. mp 276—277 °C^{5f)}; mp 278—283 °C^{5g)}). This material was identical with an authentic sample of oxyavicine.^{5g)}

7-Ethoxy-8-methoxy-5-methyl-2,3-methylenedioxybenzo[c]phenanthridin-6(5H)-one (10e)—i) The ψ -Cyanide (11e): The quaternary base (1e) chloride (0.176 g), H₂O (10 ml), and KCN (0.038 g) were heated for 1 h. Colorless prisms (0.138 g), mp 241—249 °C (CHCl₃–MeOH). *Anal.* Calcd for C₂₃H₂₀N₂O₄: C, 71.12; H, 5.19; N, 7.21. Found: C, 70.91; H, 5.09; N, 7.02. ¹H-NMR δ : 1.46 (3H, t, *J*=7.0 Hz, CH₂CH₃), 2.60 (3H, s, NCH₃), 3.90 (3H, s, OCH₃), 4.24 (2H, m, OCH₂CH₃), 5.61 (1H, s, ArCHN), 6.01 (2H, s, OCH₂O), 7.02, 7.49, 7.51, and 7.68 (each 1H, d, *J*=9.0 Hz, C₉–, C₁₂–, C₁₀–, and C₁₁–H), 7.09 and 7.61 (each 1H, s, C₁– and C₄–H).

ii) The Oxybase (10e): The ψ -cyanide (11e) (0.052 g), HMPA (2.5 ml), and NaH (0.010 g) were used. The reaction time was 2 h. Colorless prisms (0.044 g), mp 163—164.5 °C (CHCl₃–MeOH). *Anal.* Calcd for C₂₂H₁₉NO₅: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.83; H, 4.98; N, 3.71. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{–1}: 1653 (CO). ¹H-NMR δ : 1.52 (3H, t, *J*=7.0 Hz, CH₂CH₃), 3.85 (3H, s, NCH₃), 3.94 (3H, s, OCH₃), 4.25 (2H, q, *J*=7.0 Hz, OCH₂CH₃), 6.02 (2H, s, OCH₂O), 7.07 and 7.47 (each 1H, s, C₁– and C₄–H), 7.30 and 7.43 (each 1H, d, *J*=9.5 Hz, C₉– and C₁₂–H), 7.85 (2H, d, *J*=9.5 Hz, C₁₀– and C₁₁–H).

5-Methyl-2,3,7,8-bismethylenedioxybenzo[c]phenanthridin-6(5H)-one (Oxysanguinarine) (10h)—i) Sanguinarine ψ -Cyanide (11h): Sanguinarine (1h) sulfate (0.043 g), H₂O (10 ml), and KCN (0.010 g) were heated for 0.5 h. Colorless prisms (0.028 g), mp 235—239 °C (CHCl₃–MeOH) (lit.²²⁾ mp 242—243 °C). *Anal.* Calcd for C₂₁H₁₄N₂O₄: C, 70.38; H, 3.94; N, 7.82. Found: C, 70.39; H, 3.86; N, 7.80. ¹H-NMR δ : 2.64 (3H, s, NCH₃), 5.29 (1H, s, ArCHN), 6.00—6.16 (2H, m, OCH₂O), 6.02 (2H, s, OCH₂O), 6.93, 7.36, 7.53, and 7.70 (each 1H, d, *J*=8.0 Hz, C₉–, C₁₂–, C₁₀–, and C₁₁–H), 7.10 and 7.64 (each 1H, s, C₁– and C₄–H).

ii) Oxysanguinarine (10h): Sanguinarine ψ -cyanide (11h) (0.040 g), HMPA (1.5 ml), and NaH (0.015 g) were used. The reaction time was 2 h. Colorless fine needles (0.031 g), mp > 300 °C (CHCl₃–MeOH) (lit. mp 356—358 °C²²⁾; mp 360 °C^{7b)}). *Anal.* Calcd for C₂₀H₁₃NO₅: C, 69.16; H, 3.77; N, 4.03. Found: C, 69.03; H, 3.72; N, 4.05. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{–1}: 1660 (CO). ¹H-NMR δ : 3.91 (3H, s, NCH₃), 6.07 and 6.26 (each 2H, s, OCH₂O), 7.16 and 7.58 (each 1H, s, C₁– and C₄–H), 7.22, 7.53, 7.76, and 7.98 (each 1H, d, *J*=8.5 Hz, C₉–, C₁₂–, C₁₀–, and C₁₁–H).

8-Ethoxy-5-ethyl-7-methoxy-2,3-methylenedioxybenzo[c]phenanthridin-6(5H)-one (10k)—i) The ψ -Cyanide (11k): The quaternary base (1k) chloride (0.087 g), aqueous MeOH [MeOH (2 ml) and H₂O (6 ml)], and KCN (0.021 g) were heated for 1 h. Colorless prisms (0.066 g), mp 207—210 °C (MeOH–CHCl₃). *Anal.* Calcd for C₂₄H₂₂N₂O₄: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.53; H, 5.65; N, 7.22. ¹H-NMR δ : 1.16 and 1.49 (each 3H, t, *J*=

7.0 Hz, CH_2CH_3), 2.86 (2H, q, $J=7.0$ Hz, NCH_2CH_3), 4.04 (3H, s, OCH_3), 4.16 (2H, q, $J=7.0$ Hz, OCH_2CH_3), 5.84 (1H, s, ArCHN), 6.04 (2H, s, OCH_2O), 7.02 and 7.71 (each 1H, d, $J=8.5$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{11}\text{-H}$), 7.12 and 7.61 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$), 7.53 (2H, d, $J=8.5$ Hz, $\text{C}_{10}\text{-}$ and $\text{C}_{12}\text{-H}$).

ii) The Oxybase (**10k**): The ψ -cyanide (**11k**) (0.074 g), HPMA (1 ml), and NaH (0.013 g) were used. The reaction time was 2.5 h. Colorless fine needles (0.057 g), mp 177–179 °C ($\text{CHCl}_3\text{-MeOH}$). *Anal.* Calcd for $\text{C}_{23}\text{H}_{21}\text{NO}_5$: C, 70.57; H, 5.41; N, 3.58. Found: C, 70.57; H, 5.51; N, 3.89. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1650 (CO). $^1\text{H-NMR}$ δ : 1.45 and 1.47 (each 3H, t, $J=7.0$ Hz, CH_2CH_3), 4.09 (3H, s, OCH_3), 4.18 (2H, q, $J=7.0$ Hz, OCH_2CH_3), 4.42 (2H, q, $J=7.0$ Hz, NCH_2CH_3), 6.03 (2H, s, OCH_2O), 7.09 and 7.44 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$), 7.30 and 7.43 (each 1H, d, $J=9.0$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{12}\text{-H}$), 7.86 and 7.90 (each 1H, d, $J=9.0$ Hz, arom. H).

7-Ethoxy-5-ethyl-8-methoxy-2,3-methylenedioxybenzo[c]phenanthridin-6(5H)-one (10l)—i) The ψ -Cyanide (**11l**): The quaternary base (**11**) chloride (0.103 g), H_2O (5 ml), and KCN (0.023 g) were heated for 1 h. Colorless prisms (0.073 g), mp 215–225 °C ($\text{CHCl}_3\text{-MeOH}$). *Anal.* Calcd for $\text{C}_{24}\text{H}_{22}\text{N}_2\text{O}_4$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.97; H, 5.70; N, 7.08. $^1\text{H-NMR}$ δ : 1.13 and 1.45 (each 3H, t, $J=7.0$ Hz, CH_2CH_3), 2.83 (2H, dif. q, $J=7.0$ Hz, NCH_2CH_3), 3.87 (3H, s, OCH_3), 4.22 (2H, m, OCH_2CH_3), 5.78 (1H, s, ArCHN), 5.98 (2H, s, OCH_2O), 6.97 and 7.65 (each 1H, d, $J=9.0$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{11}\text{-H}$), 7.06 and 7.54 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$), 7.46 and 7.48 (each 1H, d, $J=9.0$ Hz, arom. H).

ii) The Oxybase (**10l**): The ψ -cyanide (**11l**) (0.053 g), HMPA (2.5 ml), and NaH (0.010 g) were used. The reaction time was 4 h. Slightly brown needles (0.040 g), mp 162–164 °C ($\text{CHCl}_3\text{-MeOH}$). *Anal.* Calcd for $\text{C}_{23}\text{H}_{21}\text{NO}_5$: C, 70.57; H, 5.41; N, 3.58. Found: C, 70.30; H, 5.38; N, 3.61. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1650 (CO). $^1\text{H-NMR}$ δ : 1.37 and 1.50 (each 3H, t, $J=7.0$ Hz, CH_2CH_3), 3.92 (3H, s, OCH_3), 4.25 (2H, q, $J=7.0$ Hz, OCH_2CH_3), 4.43 (2H, q, $J=7.0$ Hz, NCH_2CH_3), 6.01 (2H, s, OCH_2O), 7.08 and 7.41 (each 1H, s, $\text{C}_1\text{-}$ and $\text{C}_4\text{-H}$), 7.29 and 7.42 (each 1H, d, $J=9.0$ Hz, $\text{C}_9\text{-}$ and $\text{C}_{12}\text{-H}$), 7.85 and 7.88 (each 1H, d, $J=9.0$ Hz, arom. H).

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