Chemical Transformation of Protoberberines. XVII.[1] Biomimetic Introduction of an Oxy Functionality at the C-10 Position in the Benzo[*c*]phenanthridine Skeleton: Synthesis of 2,3,7,8,10-Pentaoxygenated Benzo[*c*]phenanthridine Alkaloids, Chelilutine and Sanguilutine[2]

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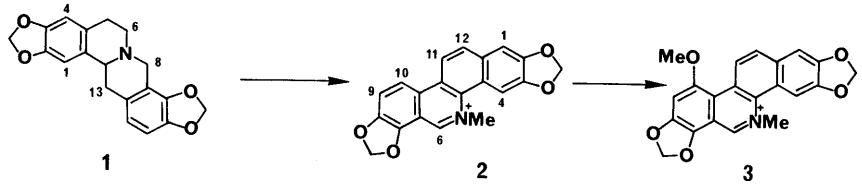
An efficient and biomimetic introduction of an oxy functionality at the C-10 position in the benzo[*c*]phenanthridine skeleton was developed by regioselective oxygenation with salcomine-oxygen. This biomimetic procedure was successfully applied to a synthesis of 2,3,7,8,10-pentaoxygenated benzo[*c*]phenanthridine alkaloids, chelilutine (8) and sanguilutine (18), from the corresponding 2,3,7,8-tetraoxygenated benzo[*c*]phenanthridines.

Keywords benzo[*c*]phenanthridine alkaloid; protoberberine; regioselective oxygenation; biomimetic transformation; salcomine; chelilutine; sanguilutine; *p*-quinone

Recent biosynthetic studies[3] on chelirubine (**3**), a representative 2,3,7,8,10-pentaoxygenated benzo[*c*]phenanthridine alkaloid[4] have disclosed that the methoxy group at the C-10 position in **3** is introduced after formation of the corresponding 2,3,7,8-tetraoxygenated benzo[*c*]phenanthridine alkaloid, sanguinarine (**2**), which is biosynthesized from the protoberberine alkaloid stylopine (**1**)[3,5] through C_6–N bond fission and recyclization between the C-6 and C-13 positions. This intriguing biogenetic pathway has led us to explore a direct method for the introduction of the methoxy group at the C-10 position in the 2,3,7,8-tetraoxygenated benzo[*c*]phenanthridine skeleton.

In connection with our recent results[1,6-8] on biomimetic synthesis of benzo[*c*]phenanthridine alkaloids from their biogenetic precursors, protoberberine alkaloids, we thought that a convenient transformation of 2,3,7,8-tetraoxygenated benzo[*c*]phenanthridines into the corresponding 2,3,7,8,10-pentaoxygenated ones would open up a new aspect of the chemistry of benzo[*c*]phenanthridine alkaloids, even though some syntheses of the pentaoxygenated compounds have already been reported.[8-11] We chose 7-*O*-demethyldihydrochelerythrine (**4**)[6b] as a suitable substrate for our purpose because the C_7-hydroxy group in **4** would be expected to make oxidation at the C-10 position much easier through the *p*-quinone derivative, which should be convertible into the desired trimethoxy compound. We describe here a novel and biomimetic synthesis of chelilutine (**8**) and sanguilutine (**18**) from the 2,3,7,8-tetraoxygenated benzo[*c*]phenanthridines by the use of salcomine-oxygen oxidation as a key step.

Several oxidants, including cerium ammonium nitrate (CAN),[12] iodosobenzene,[13] Fremy's salt,[14] and salcomine-oxygen,[15] are able to convert a phenol group into a *p*-quinone derivative. However, the former two reagents oxidized the tertiary amine moiety of **4** in preference to the phenol group to produce the quaternary salt rather than the *p*-quinone compound. Fremy's salt did not work in this case. Finally salcomine-oxygen was found to be the best oxidant for our purpose. Thus, **4** was treated with salcomine in tetrahydrofuran (THF) at room temperature in a stream of oxygen to afford the *p*-quinone derivative (**5**) in 94% yield. The structure of **5** was easily elucidated on the basis of spectral evidence. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **5** showed the downfield-shifted C-11 proton signal at δ 8.15 ppm (the C-11 proton signal of the starting **4** appeared at δ 7.75 ppm[6b]) as a doublet, as well as the C-9 proton signal at δ 5.97 ppm as a singlet. Furthermore, **5** showed infrared (IR) absorptions at 1650 and 1620 cm^{-1} due to the *p*-quinone moiety. It is noteworthy that no reaction took place when 7-*O*-demethyloxychelerythrine (**4'**) instead of 7-*O*-demethyldihydrochelerythrine (**4**) was exposed to salcomine-oxygen. The *p*-quinone moiety in **5** was then reduced with sodium hydrosulfite in aqueous acetone at room temperature. The reaction was monitored by thin-layer chromatography (TLC), which revealed consumption of the starting material and the appearance of a new product, presumably the 7,10-dihydroxy-8-methoxy derivative (**6**). However, isolation of **6** was troublesome, in spite of its easy formation. The dihydroxy compound (**6**) could not be purified because it was extremely susceptible to oxidation during work-up to regenerate partially the starting *p*-quinone (**5**). Therefore, the crude product was immediately methylated with diazomethane to afford dihydrochelilutine (**7**) in 53% yield from **5** (method A). Although **7** could thus be obtained from **5**, the yield was not satisfactory. Accordingly an alternative and more efficient procedure (method B) was developed. The *p*-quinone (**5**) was catalytically hydrogenated over palladium on carbon (Pd–C) in the presence of dimethyl sulfate[16] in an alkaline solution to provide **7** in 81% yield. The latter procedure (method B) was much easier and more efficient than the former one (method A). Dihydrochelilutine was finally converted into chelilutine (**8**)



1 2 3

Chart 1

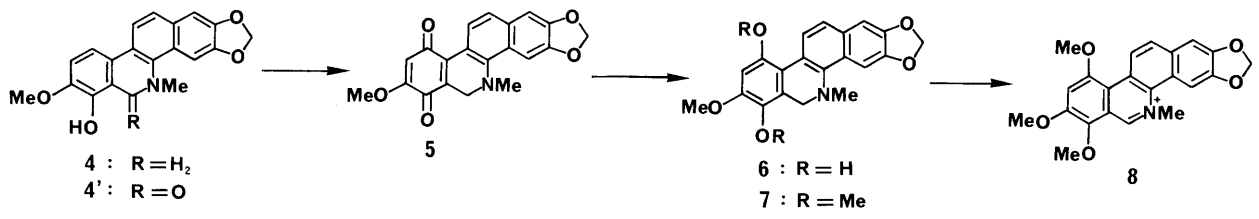
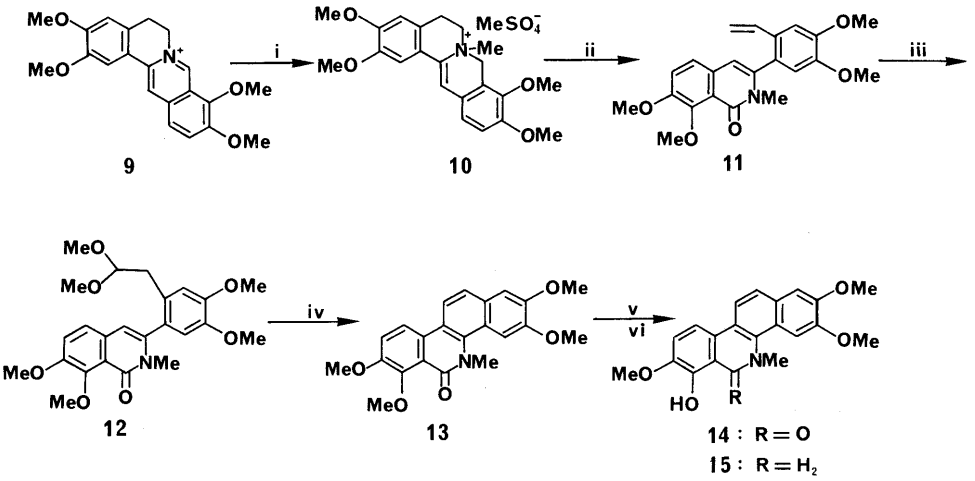


Chart 2



i) a: LAH–THF, b: Me_2SO_4–C_6H_6 (94%); ii) a: 25% KOH–MeOH, b: DDQ–$CHCl_3$ (31%); iii) $Tl(NO_3)_3$–MeOH (91%); iv) 10% HCl–MeOH (96%); v) *p*-TsOH–toluene (90%); vi) a: LAH–THF, b: $NaBH_4$–MeOH (86%).

Chart 3

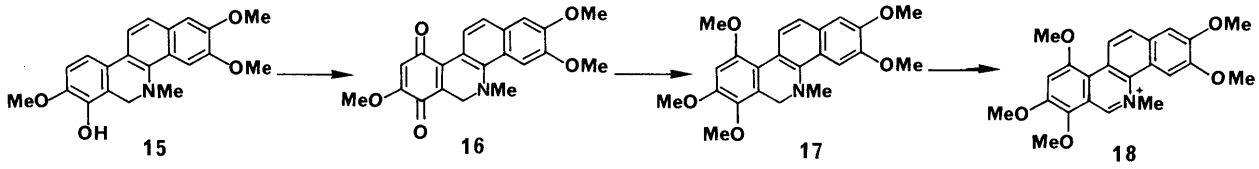


Chart 4

by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation. The synthetic chelilutine was identical with natural chelilutine by spectral comparison. Thus, we succeeded in synthesizing chelilutine (**8**) from **4** *via* a biomimetic procedure.

The next step in this investigation was to examine the generality of the above reaction. We therefore applied it to a biomimetic synthesis of sanguilutine (**18**),[8] a 2,3,7,8,10-pentamethoxybenzo[*c*]phenanthridine alkaloid. The required 7-hydroxybenzo[*c*]phenanthridine (**15**) was prepared according to our procedure[6] described previously for the synthesis of **4**. Palmatine (**9**) was converted to the 3-arylisoquinolone (**11**) *via* the methosulfate (**10**). Successive exposure of **11** to thallium trinitrate (TTN) and 10% hydrochloric acid afforded the benzo[*c*]phenanthridine (**13**). The regioselective demethylation of the C_7-methoxy group in **13** was achieved by heating in toluene in the presence of *p*-toluenesulfonic acid (*p*-TsOH) to furnish the phenol (**14**), reduction[6a] of which yielded the 7-hydroxy derivative (**15**). The results are summarized in Chart 3.

Application of salcomine-oxygen oxidation to **15** effected regioselective introduction of an oxy functionality at the C-10 position to produce the *p*-quinone (**16**) in 94% yield. Consecutive hydrogenation of **16** and methylation gave dihydrosanguilutine (**17**, 90%), which was identical with an authentic specimen[8] by spectral comparison. Since dihydrosanguilutine has already been converted into sanguilutine (**18**),[8] the present synthesis amounts to a formal synthesis of **18**.

Thus, we have completed a synthesis of chelilutine and sanguilutine from the corresponding 2,3,7,8-tetraoxygenated benzo[*c*]phenanthridines through the putative biosynthetic pathway. Although we had previously explored a method for the synthesis of 2,3,7,8,10-pentaoxygenated benzo[*c*]phenanthridine alkaloids[1,8] from the corresponding 2,3,8,9,10-pentaoxygenated protoberberines, the present convenient conversion provides an alternative and effective method for the preparation of 2,3,7,8,10-pentaoxygenated benzo[*c*]phenanthridine alkaloids. In the previous paper,[1] we described the regioselective oxygenation at C-12 of 2,3,7,8,10-pentaoxygenated alkaloid, therefore, the present conversion implies that we could accomplish a biomimetic transformation of the protoberberine alkaloids into all types of benzo[*c*]phenanthridine alkaloids according to the following sequences: protoberberine→2,3,7,8-tetraoxygenated[6]→2,3,7,8,10-pentaoxygenated→2,3,7,8,10,12-hexaoxygenated benzo[*c*]phenanthridine alkaloid.[1]

Experimental

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Alumina (Aluminiumoxid 90, Aktivitätsstufe II—III, 70—230 mesh, Merck) and silica gel (Kieselgel 60, 70—230 mesh, Merck) were used for column chromatography. Organic extracts were dried over anhydrous Na_2SO_4. IR spectra were measured with a JASCO A-102 spectrometer in $CHCl_3$, mass spectra (MS) with a Hitachi M-80 mass spectrometer, ultraviolet (UV) spectra with a Hitachi U-3200 spectrophotometer, and ^{1}H-NMR spectra with a JEOL FX-100 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard, unless otherwise stated.

5,6,7,10-Tetrahydro-8-methoxy-5-methyl-2,3-methylenedioxy-7,10-dioxobenzo[*c*]phenanthridine (5) Salcomine (101 mg, 0.31 mmol) was added to a solution of 7-*O*-demethyldihydrochelerythrine (**4**)[6b] (104 mg, 0.31 mmol) in dry THF (20 ml) in a stream of oxygen at room temperature. After being stirred for 2 h at room temperature, the reaction mixture was concentrated and the residue was passed through Florisil with CH_2Cl_2–MeOH (100 : 3) to afford **5** (102 mg, 94%), dark brown needles, mp 198—205 °C (dec.) (CH_2Cl_2–hexane). IR ν_{max} cm^{-1}: 1650, 1620 (*p*-quinone). UV λ_{max}^{MeOH} nm (log ε): 347 (3.83), 327 (3.89), 265 (4.49), 237 (4.50). ^{1}H-NMR δ: 8.15, 7.46 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 7.57, 7.27 (each 1H, each s, C_4-H, C_1-H), 6.08 (2H, s, OCH_2O), 5.97 (1H, s, C_9-H), 4.14 (2H, s, C_6-H), 3.87 (3H, s, OMe), 2.69 (3H, s, NMe). MS *m/z* (%): 351 (M^++2,[17] 67), 350 (M^++1, 50), 349 (M^+, 70), 84 (45), 49 (100). *Anal.* Calcd for $C_{20}H_{15}NO_5$: C, 68.76; H, 4.33; N, 4.01. Found: C, 68.56; H, 4.37; N, 3.99.

Dihydrochelilutine (7) Method A: A saturated aqueous $Na_2S_2O_4$ solution (5 ml) was added to a stirred solution of **5** (148 mg, 0.42 mmol) in acetone (15 ml) at room temperature and stirring was continued for an additional hour. The reaction mixture was diluted with CH_2Cl_2 and the CH_2Cl_2 layer was washed with water and brine, dried, and concentrated. The residue was immediately dissolved in MeOH (10 ml) under an argon atmosphere. A solution of diazomethane in ether was added to the MeOH solution at −20 °C. The reaction mixture was allowed to stand at the same temperature for 3 h, then quenched by addition of a small amount of acetic acid. The solvent was evaporated off to leave the residue, which was chromatographed on silica gel with CH_2Cl_2 to give **7** (85 mg, 53%), mp 145—147 °C (MeOH) (lit.[11] 139—142 °C). UV λ_{max}^{MeOH} nm (log ε): 327 (4.25), 279 (4.60), 230 (4.56). ^{1}H-NMR δ: 8.29, 7.45 (each 1H, ABq, J=8.7 Hz, C_{11}-H, C_{12}-H), 7.69, 7.10, 6.57 (each 1H, each s, C_4-H, C_1-H, C_9-H), 6.03 (2H, s, OCH_2O), 4.21 (2H, s, C_6-H), 3.95, 3.92, 3.82 (each 3H, each s, OMe × 3), 2.56 (3H, s, NMe). MS *m/z* (%): 379 (M^+, 100), 348 (47), 306 (27). *Anal.* Calcd for $C_{22}H_{21}NO_5$: C, 69.64; H, 5.58; N, 3.69. Found: C, 69.71; H, 5.52; N, 3.66.

Method B: A solution of **5** (128 mg, 0.37 mmol) in dimethylformamide (15 ml) was vigorously stirred with 5% Pd–C (61 mg) under 1 atm pressure of hydrogen at room temperature for 1 h, then $Ba(OH)_2 \cdot 8H_2O$ (579 mg, 1.84 mmol) and dimethyl sulfate (0.17 ml, 1.84 mmol) were added at once to the reaction mixture. Hydrogenation was continued for an additional 2 h. The solvent was evaporated off to leave the residual oil, to which a small amount of water and aqueous ammonia were added, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue furnished **7** (112 mg, 81%).

Chelilutine Chloride (8) A solution of DDQ (54 mg, 0.24 mmol) was added to a vigorously stirred mixture of **7** (60 mg, 0.16 mmol) and 5% aqueous sodium hydroxide (1 ml) in benzene (5 ml) at room temperature for 3 h. The benzene layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layers were washed with water and brine, dried, and concentrated to dryness. The residue was dissolved in a small amount of acetone, and concentrated hydrochloric acid was added. The resulting precipitates were collected by filtration and recrystallized from MeOH to give **8** (59 mg, 90%), mp 194—195 °C (lit. 184—186 °C,[11] 197—198 °C (dec.)[9]). IR ν_{max} cm^{-1}: 1620 (N=C). UV λ_{max}^{MeOH} nm (log ε): 334 (4.27), 278 (4.57), 230 (4.50). ^{1}H-NMR ($(CD_3)_2SO$) δ: 10.04 (1H, s, C_6-H), 9.39, 8.23 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 8.21, 7.77, 7.73 (each 1H, each s, C_4-H, C_1-H, C_9-H), 6.34 (2H, s, OCH_2O), 4.95 (3H, s, NMe), 4.27, 4.17, 4.09 (each 3H, each s, OMe × 3). *Anal.* Calcd for $C_{22}H_{20}ClNO_5 \cdot 5/2H_2O$: C, 57.58; H, 5.49; N, 3.05. Found: C, 57.62; H, 5.18; N, 3.11.

5,6,7,8-Tetrahydro-2,3,9,10-tetramethoxy-7-methyldibenzo[*a*,*g*]quinolizinium Monomethylsulfate (10) Palmatine iodide (**9**, 7.0 g, 14.6 mmol) was added portionwise to a stirred suspension of lithium aluminum hydride (LAH) (1.67 g, 43.8 mmol) in dry THF (150 ml) over a period of 15 min in a stream of nitrogen at 0 °C. The suspension was stirred for 2 h at room temperature, then water was added to the suspension and the whole was filtered. The filtrate was concentrated to leave the crude dihydro derivative, which was dissolved in hot benzene (150 ml). Dimethyl sulfate (4.15 ml, 43.8 mmol) was added dropwise to the refluxing benzene solution and refluxing was continued for 2 h. After cooling of the reaction mixture to room temperature, the resulting precipitates were collected by filtration and dried to provide **10** (6.6 g, 94%), pale yellow cubes, mp 247—249 °C (MeOH). UV λ_{max}^{MeOH} nm (log ε): 350 (4.54), 250 (4.13), 214 (4.42). ^{1}H-NMR ($(CD_3)_2SO$) δ: 7.78, 7.43, 6.93 (each 1H, each s, C_4-H, C_1-H, C_{13}-H), 7.31, 7.23 (each 1H, ABq, J=8.5 Hz, C_{12}-H, C_{11}-H), 5.11, 4.88 (each 1H, ABq, J=15 Hz, C_8-H), 4.27—3.95 (2H, m, C_6-H), 3.91, 3.86, 3.84, 3.83 (each 3H, each s, OMe × 4), 3.40—3.10 (2H, m, C_5-H), 3.38 (3H, s, $MeSO_4$), 3.06 (3H, s, NMe). *Anal.* Calcd for $C_{23}H_{29}NO_8S \cdot H_2O$: C, 55.52; H, 6.28; N, 2.82. Found: C, 55.87; H, 6.03; N, 2.81.

7,8-Dimethoxy-3-(4,5-dimethoxy-2-vinylphenyl)-2-methylisoquinolin-1(2*H*)-one (11) The methosulfate (**10**) (3.0 g, 6.24 mmol) was added in one portion to refluxing 25% methanolic potassium hydroxide (20 ml) and the mixture was heated under reflux for 10 min, then poured into ice-water (40 ml) and extracted with chloroform (150 ml). The extract was washed with water and brine, and dried. DDQ (2.0 g, 8.73 mmol) was added to the above solution and the mixture was stirred for 17 h at room temperature. The chloroform solution was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue on silica gel with CH_2Cl_2–MeOH (100 : 1) afforded **11** (740 mg, 31%), pale yellow pillars, mp 165.5—166.5 °C (CH_2Cl_2–iso-Pr_2O). IR ν_{max} cm^{-1}: 1650 (amide). UV λ_{max}^{MeOH} nm (log ε): 354 (3.94), 299 (4.30), 267 (4.27), 224 (4.72). ^{1}H-NMR δ: 7.35, 7.18 (each 1H, ABq, J=8.8 Hz, aromatic H), 7.15, 6.75, 6.31 (each 1H, each s, aromatic H), 6.50 (1H, dd, J=17, 11 Hz, vinylic H), 5.62 (1H, dd, J=17, 1 Hz, vinylic H), 5.15 (1H, dd, J=11, 1 Hz, vinylic H), 4.03, 3.98, 3.96, 3.89 (each 3H, each s, OMe × 4), 3.24 (3H, s, NMe). MS *m/z* (%): 381 (M^+, 100), 366 (61), 352 (30). *Anal.* Calcd for $C_{22}H_{23}NO_5$: C, 69.27; H, 6.08; N, 3.67. Found: C, 69.31; H, 6.12; N, 3.86.

7,8-Dimethoxy-3-[4,5-dimethoxy-2-(2,2-dimethoxyethyl)phenyl]-2-methylisoquinolin-1(2*H*)-one (12) A solution of TTN trihydrate (187 mg, 0.42 mmol) in MeOH (10 ml) was added dropwise to a solution of **11** (133 mg, 0.35 mmol) in MeOH (20 ml) at room temperature and the reaction mixture was stirred for 15 min, then filtered. A saturated aqueous sodium bicarbonate solution (10 ml) was added to the filtrate and the mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue on silica gel with CH_2Cl_2–MeOH (100 : 1) gave **12** (140 mg, 91%) as an oil. IR ν_{max} cm^{-1}: 1650 (amide). ^{1}H-NMR δ: 7.34, 7.22 (each 1H, ABq, J= 9.0 Hz, aromatic H), 6.96, 6.73, 6.31 (each 1H, each s, aromatic H), 4.42 (1H, dd, J=6.0, 5.0 Hz, C$\underline{H}$$CH_2$), 4.03, 3.96, 3.92, 3.87 (each 3H, each s, OMe × 4), 3.26, 3.25 (each 3H, each s, OMe × 2), 3.21 (3H, s, NMe), 2.90 (1H, dd, J=14, 6.0 Hz, CHC$\underline{H}_2$), 2.66 (1H, dd, J=14, 5.0 Hz, CHC$\underline{H}_2$). MS *m/z* (%): 443 (M^+, 41%), 368 (23), 75 (100). High-resolution MS calcd for $C_{24}H_{29}NO_7$: 443.1942. Found: 443.1942.

2,3,7,8-Tetramethoxy-5-methylbenzo[*c*]phenanthridin-6(5*H*)-one (13) A solution of **12** (245 mg, 0.55 mmol) and 10% hydrochloric acid (5 ml) in MeOH (20 ml) was refluxed for 30 min, then MeOH was evaporated off and the residue was taken up in CH_2Cl_2. The solution was washed with water and brine, dried, and concentrated to leave the residue, which was chromatographed on silica gel with CH_2Cl_2–MeOH (100 : 1) to give **13** (202 mg, 96%), colorless needles, mp 221—223 °C (MeOH). IR ν_{max} cm^{-1}: 1640 (amide). UV λ_{max}^{MeOH} nm (log ε): 323 (4.20), 286 (4.81), 277 (4.70), 241 (4.61). ^{1}H-NMR δ: 8.00, 7.56 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 7.99, 7.39 (each 1H, ABq, J=9.0 Hz, C_{10}-H, C_9-H), 7.51, 7.16 (each 1H, each s, C_4-H, C_1-H), 4.09, 4.08, 4.03, 3.98 (each 3H, each s, OMe × 4), 3.96 (3H, s, NMe). MS *m/z* (%): 379 (M^+, 100), 364 (37), 350 (20). *Anal.* Calcd for $C_{22}H_{21}NO_5$: C, 69.64; H, 5.58; N, 3.69. Found: C, 69.71; H, 5.55; N, 3.77.

7-Hydroxy-2,3,8-trimethoxy-5-methylbenzo[*c*]phenanthridin-6(5*H*)-one (14) A solution of **13** (283 mg, 0.75 mmol) and *p*-TsOH (213 mg, 1.12 mmol) in toluene (30 ml) was heated under reflux for 3.5 h. After cooling, the solvent was evaporated off and the residue was taken up in CH_2Cl_2. The solution was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue on silica gel with CH_2Cl_2–MeOH (100 : 1) provided **14** (245 mg, 90%), pale yellow needles, mp 220—221 °C (MeOH). IR ν_{max} cm^{-1}: 3545 (OH), 1640 (amide). UV λ_{max}^{MeOH} nm (log ε): 344 (4.21), 331 (4.17), 285 (4.73), 244 (4.67). ^{1}H-NMR δ: 8.00, 7.58 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 7.64, 7.33 (each 1H, ABq, J=9.0 Hz, C_{10}-H, C_9-H), 7.51, 7.16 (each 1H, each s, C_4-H, C_1-H), 4.04 (3H, s, OMe), 4.00 (6H, s, OMe × 2), 3.99 (3H, s, NMe), 3.35 (1H, s, OH).

MS *m/z* (%): 365 (M^+, 100), 350 (43), 322 (20). *Anal.* Calcd for $C_{21}H_{19}NO_5$: C, 69.03; H, 5.24; N, 3.83. Found: C, 68.94; H, 5.23; N, 3.90.

5,6-Dihydro-7-hydroxy-2,3,8-trimethoxy-5-methylbenzo[*c*]phenanthridine (15) LAH (121 mg, 3.18 mmol) was added to a stirred solution of **14** (116 mg, 0.32 mmol) in dry THF (20 ml) in a stream of nitrogen at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was diluted with water and filtered. The filtrate was concentrated and the residue was dissolved in MeOH (20 ml). Sodium borohydride (121 mg, 3.18 mmol) was added portionwise to the above solution. The reaction mixture was stirred at room temperature for 30 min, then MeOH was evaporated off. The residue was taken up in CH_2Cl_2. The solution was washed with water and brine, dried, and concentrated to dryness. Chromatography of the residue on alumina with CH_2Cl_2 gave **15** (96 mg, 86%), colorless needles, mp 98—100 °C (MeOH). IR ν_{max} cm^{-1}: 3550 (OH). UV λ_{max}^{MeOH} nm (log ε): 321 (4.21), 281 (4.64), 234 (4.53). ^{1}H-NMR δ: 7.72, 7.50 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 7.67, 7.12 (each 1H, each s, C_4-H, C_1-H), 7.21, 6.99 (each 1H, ABq, J=8.0 Hz, C_{10}-H, C_9-H), 5.70 (1H, s, OH), 4.33 (2H, s, C_6-H), 4.07, 4.01, 3.93 (each 3H, each s, OMe × 3), 2.64 (3H, s, NMe). MS *m/z* (%): 351 (M^+, 100), 350 (67). *Anal.* Calcd for $C_{21}H_{21}NO_4 \cdot 1/2MeOH$: C, 69.79; H, 6.42; N, 3.88. Found: C, 69.79; H, 6.42; N, 3.87.

5,6,7,10-Tetrahydro-2,3,8-trimethoxy-5-methyl-7,10-dioxobenzo[*c*]phenanthridine (16) According to the procedure described for **4**, the hydroxy derivative (**15**) (79 mg, 0.23 mmol) was treated with salcomine (73 mg, 0.23 mmol) in a stream of oxygen to give, after passage through Florisil with CH_2Cl_2–MeOH (100 : 3), **16** (77 mg, 94%), dark brown needles, mp 197—203 °C (dec.) (CH_2Cl_2–hexane). IR ν_{max} cm^{-1}: 1650, 1620 (*p*-quinone). UV λ_{max}^{MeOH} nm (log ε): 347 (3.84), 326 (3.86), 263 (4.56), 240 (4.52). ^{1}H-NMR δ: 8.17, 7.50 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 7.54, 7.11, 5.96 (each 1H, each s, C_4-H, C_1-H, C_9-H), 4.16 (2H, s, C_6-H), 4.05, 4.02, 3.87 (each 3H, each s, OMe × 3), 2.72 (3H, s, NMe). MS *m/z* (%): 367 (M^+ +2,[17] 56), 366 (M^+ +1, 46), 365 (M^+, 100), 350 (32), 322 (30). *Anal.* Calcd for $C_{21}H_{19}NO_5$: C, 69.03; H, 5.24; N, 3.83. Found: C, 69.11; H, 5.48; N, 3.61.

Dihydrosanguilutine (17) According to the procedure (method B) described for **5**, the *p*-quinone (**16**) (61 mg, 0.17 mmol) was hydrogenated on 5% Pd–C (29 mg) in the presence of $Ba(OH)_2 \cdot 8H_2O$ (274 mg, 0.83 mmol) and dimethyl sulfate (0.08 ml, 0.83 mmol) in dimethylformamide (7 ml). Work-up and chromatography on silica gel with CH_2Cl_2 afforded **17** (59 mg, 90%), colorless cubes, mp 152—154 °C (MeOH) (lit.[8] 154—155 °C). UV λ_{max}^{MeOH} nm (log ε): 326 (4.28), 277 (4.64), 228 (4.57). ^{1}H-NMR δ: 8.32, 7.48 (each 1H, ABq, J=9.0 Hz, C_{11}-H, C_{12}-H), 7.68, 7.12, 6.57 (each 1H, each s, C_4-H, C_1-H, C_9-H), 4.24 (2H, s, C_6-H), 4.07, 4.01, 3.95, 3.92, 3.82 (each 3H, each s, OMe × 5), 2.60 (3H, s, NMe). MS *m/z* (%): 395 (M^+, 100), 364 (17). *Anal.* Calcd for $C_{23}H_{25}NO_5$: C, 69.85; H, 6.37; N, 3.54. Found: C, 69.84; H, 6.57; N, 3.63.

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References and Notes

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