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Total Synthesis of the Marine Pentacyclic Alkaloid Meridine

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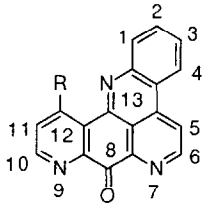
Abstract : The synthesis of the marine pyridoacridine alkaloid meridine (**1**) has been accomplished in eight steps from 2,5- dimethoxy-3-nitroaniline in 9 % overall yield.

Marine organisms constitute a source of natural products in which unique biologically active structures account for the continuing interest in these compounds.[1] Meridine **1**, a marine alkaloid was isolated by Schmitz *et al*. from the ascidian *Amphicarpa meridiana*.[2] For our part, we recently reported on the isolation and structure elucidation of cystodamine **2**, another structurally related novel pentacyclic alkaloid from the Mediterranean ascidian *Cystodytes dellechiajei*.[3] Because of the general cytotoxicity of this family, and the few biological studies on meridine,[4] we were interested in devising a synthesis of this compound that would generate intermediates that might possess potential anti-tumor properties. The recently reported synthesis of **1** by Kitahara *et al*.[5] based on an hetero-Diels-Alder strategy prompts us to report our quite different approach.



1, R = OH
2, R = NH_2

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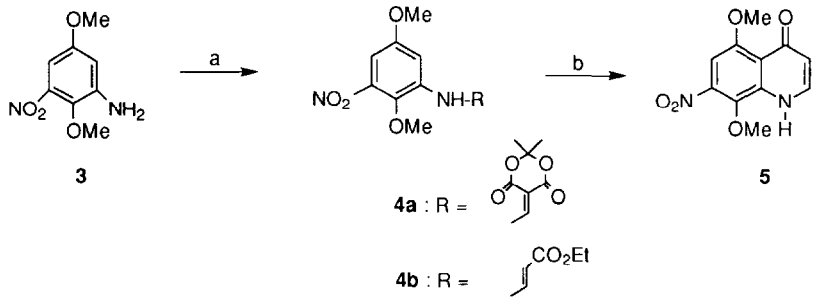
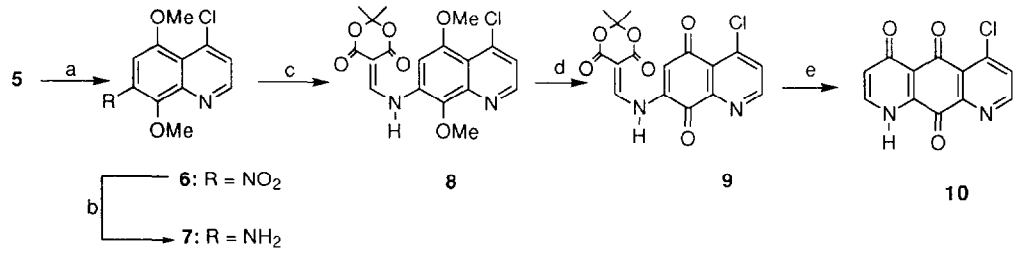
As starting material, 2,5-dimethoxy-3-nitroaniline **3** was obtained by catalytic hydrogenation (the hydrogen donor being cyclohexene) of the corresponding dinitro derivative[6] which was prepared from diacetylhydroquinone according to the published three-step procedure.[7]



a) Meldrum's acid, $HC(OEt)_3$, reflux, 2 h or ethyl propiolate, MeOH, reflux 60 h. b) diphenyl ether, N_2, reflux, 15 min.

The quinolone **5** can be produced in equal yield (83 %) either by thermal cyclization of the anilinoacrylate **4b** prepared by Michael-type addition of compound **3** with methyl propiolate[8] or by thermolysis of the arylaminomethylene Meldrum's acid derivative **4a** synthesized according to the Cassis method.[9] This latter procedure was preferred, the Meldrum derivative precipitating in the reaction medium whereas a chromatographic purification step was necessary to obtain the intermediate **4b** by the other method. In both cases, the ring closure was effected in a large amount of high boiling solvent such as diphenylether to prevent polymerization.

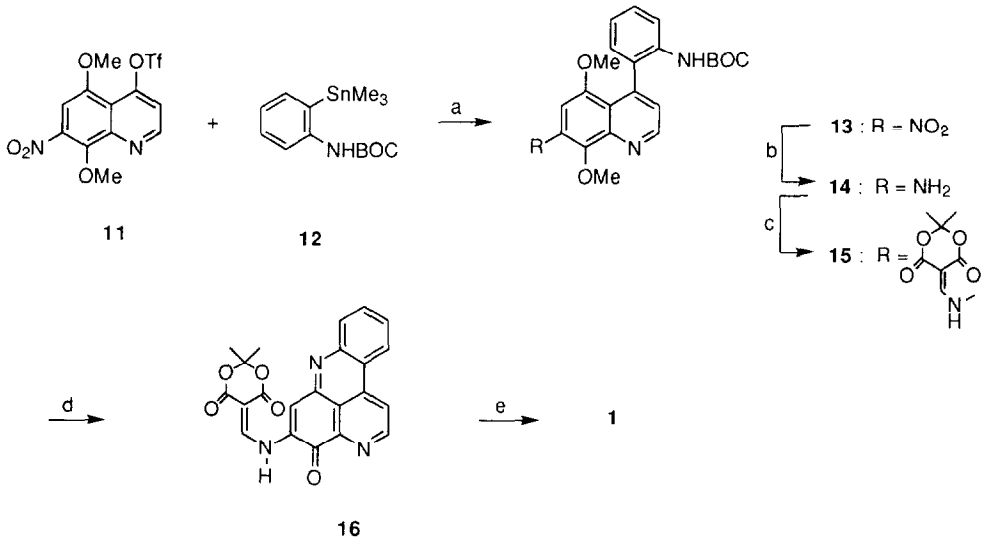
The first investigated synthetic route was based on the formation of the linear tricycle **10.**



a) $SOCl_2$, reflux, 30 min. b) $TiCl_3$, H_2O/AcOH, 20 °C, 15 min. c) Meldrum's acid, $HC(OEt)_3$, reflux, 2h. d)CAN, CH_3CN/H_2SO_4 2M, 20 °C, 15 min. e) diphenyl ether, N_2, reflux,15 min.

Treatment of **5** with $SOCl_2$ gave the chloroquinoline **6** from which the nitro function was selectively reduced by $TiCl_3$ in 90 % yield.[10] The formation of the third cycle was amorced by addition of Meldrum's acid/triethyl orthoformate to **7**. After different unsuccessful assays in direct cyclization of compound **8**, the compound **10** was obtained by cyclisation in diphenylether of the quinone **9** resulting in the oxidation of the methoxy functions. This strategy was abandoned consequently to the failure in Stille coupling of this tricyclic compound with arylstannane **12**.[11]

Reaction of trifluoromethanesulfonic anhydride, in presence of 2,6-lutidine and a catalytic amount of 4-(dimethylamino)pyridine on the quinoline **5** furnished triflate **11** in 78 % yield. The arylquinoline **13** was isolated in 92 % yield by addition at 100 °C of compound **12** under the coupling conditions used by Gômez-Bengoa and Echavarren for similar system [$Pd(PPh_3)_4$, LiCl, CuBr, dioxane].[12] The reduction of the nitro group of **13** by cyclohexene with Pd/C catalyst in refluxing methanol afforded in good yield the corresponding amino derivative **14** which was treated with Meldrum's acid and triethyl orthoformate to provide the intermediate **15**.



a) Pd(0), LiCl, CuBr, dioxane,N_2, reflux, 12 h. b) Pd/C, cyclohexene, ethanol, reflux, 45 min. c) Meldrum's acid, $HC(OEt)_3$, reflux, 2 h. d) CAN, CH_3CN/H_2SO_4 2M, 20 °C, 30 min. e) diphenyl ether, N_2, reflux, 5min.

The next step consisted in the cyclization of the Meldrum's acid derivative to the expected pentacyclic compound. As previously determined for the synthesis of compound **10**, the ring closure was undertaken after preliminary oxidation of the methoxy functions. This oxidation of derivative **15** with ammonium cerium(IV)nitrate (CAN) in acidic solution gave directly in 60 % yield the tetracyclic derivative **16** resulting from hydrolysis of the BOC-amino group and subsequent cyclization. Thermolysis of **16** in diphenylether afforded meridine **1**, the spectroscopic data of which were identical to the values reported for the natural product[2]. The

overall yield of this synthesis was 9 % which constitutes a serious improvement of the method described by Kitahara *et al.*.[5]

The transformation of meridine **1** into cystodamine **2** is presently in progress.

Experimental Section

General. All commercial chemicals were used as obtained without further purification and all solvents were carefully dried and distilled by standard methods prior to use. Column chromatography was carried out on silica gel 60 (230-400 mesh) with the flash technique. Thin-layer chromatography was performed on E. Merck $60F_{254}$ precoated silica plates (0.25 mm layer thickness). Nuclear magnetic resonance spectra were recorded at 400 MHz for ^1H and 100 MHz for ^{13}C. Peak assignments were obtained by HMBC and HMQC. Chemical shifts are reported in δ ppm relative to $(CH_3)_4Si$ and coupling constants J are in Hz. Infrared spectra (cm^{-1}) were obtained on a FT-IR spectrometer. Melting points are uncorrected.

5-{[(2',5'-Dimethoxy-3'-nitrophenyl)amino]methylidene}-2,2-dimethyl-4,6-dioxo-1,3-dioxane (4a). A solution of 2,2-dimethyl-4,6-dioxo-1,3-dioxane (0.60 g, 4.16 mmol) in triethyl orthoformate (6 ml) was refluxed for 2 h and added to amino-derivative **3**[6] (0.70 g, 3.53 mmol). Filtration of the reaction mixture afforded a pale-yellow solid : mp 169°C, (0.95 g, 76 % yield). ^1H NMR ($CDCl_3$) 1.6 (6H, s), 3.75 (3H, s), 3.95 (3H, s), 7.05 (1H, d, J = 1.2 Hz), 7.15 (1H, d, J = 1.2 Hz), 9.60 (1H, d, J = 14.5 Hz), 11.65 (1H, d, J = 14.5 Hz). ^{13}C NMR ($CDCl_3$) 26.8, 56.0, 62.8, 89.0, 105.2, 105.9, 106.0, 133.9, 137.4, 143.9, 150.4, 155.6, 162.8, 164.7. Anal. Calcd for $C_{15}H_{16}N_2O_8$: C, 51.13 ; H, 4.54; N, 7.95. Found : C, 51.02 ; H, 4.80 ; N, 7.16.

1-(2'-Ethoxycarbonylvinyl)amino-2,5-dimethoxy-3-nitrobenzene (4b). A mixture of 2,5-dimethoxy-3-nitroaniline **3** (3.70 g, 18.7 mmol) and ethyl propiolate (2.2 ml, 20.0 mmol) in anhydrous methanol (40 ml) was refluxed for 60 h. After cooling to room temperature, the reaction mixture was filtered and the precipitate washed with ice-cold methanol. A yellow powder was obtained (3.8 g, 71% yield). ^1H NMR ($CDCl_3$) 1.20 (3H, t, J = 7 Hz), 3.75 (3H, s), 3.90 (3H, s), 4.15 (2H, q, J = 7 Hz), 4.90 (1H, d, J = 8 Hz), 6.65 (1H, s), 6.85 (1H, s), 7.10 (1H, dd, J = 12 and 8 Hz), 10.28 (NH, d, J = 12 Hz). ^{13}C NMR ($CDCl_3$) 14.1, 55.6, 59.4, 62.1, 90.8, 100.3, 103.6, 135.9, 136.9, 139.9, 143.9, 155.6, 169.3. IR ($CHCl_3$) 3304, 3033, 1671, 1610, 1543, 1238, 1283, 1187 cm^{-1}.

5,8-Dimethoxy-7-nitroquinolin-4(1*H*)-one (5). A mixture of **4a** (0.75 g, 2.13 mmol) in diphenylether (40 g) was refluxed under nitrogen for 15 min. After cooling to room temperature, petroleum ether (150 ml) was added. Filtration of the reaction mixture afforded a brown-yellow solid: mp 68°C (0.44 g, 83 % yield). ^1H NMR (DMSO-d6) 3.85 (3H, s), 3.90 (3H, s), 6.05 (1H, d, J = 6.3 Hz), 7.15 (1H, s), 7.72 (1H, dd, J = 2 and 6.3 Hz), 11.45 (1H, d, J = 2 Hz). ^{13}C NMR (CF_3COOD) 59.6, 65.5, 104.6, 115.0, 131.6, 138.4, 140.8,

144.9, 148.1, 154.7, 174.5. IR (KBr) 3080, 1630, 1584, 1210 cm^{-1}. Anal. Calcd. for $C_{11}H_{10}N_2O_5$: C, 52.80; H, 4.04; N, 11.20. Found : C, 53.24; H, 4.29; N, 10.95.

4-Chloro-5,8-dimethoxy-7-nitroquinoline (6). A solution of compound **5** (1.0 g, 4.0 mmol) in thionyl chloride (50 ml) was refluxed for 30 min. After evaporation of the excess of $SOCl_2$, the reaction mixture was partitioned between a solution of $NaHCO_3$ (10%) and AcOEt. After the usual work-up a beige powder was obtained (1 g, 92% yield). ^1H NMR ($CDCl_3$) 3.85 (3H, s), 4.10 (3H, s), 7.15 (1H, s), 7.45 (1H, d, J = 5 Hz), 8.75 (1H, d, J = 5 Hz). ^{13}C NMR ($CDCl_3$) 56.3, 64.1, 100.7, 122.0, 125.9, 142.1, 142.5, 144.2, 146.3, 150.4, 152.2. IR ($CHCl_3$) 3035, 1619, 1610, 1570, 1360, 1251 cm^{-1}. Anal. Calcd. for $C_{11}H_9N_2O_4Cl$: C, 49.17; H, 3.38; N, 10.43. Found : C, 48.62; H, 3.38; N, 9.66.

7-Amino-4-chloro-5,8-dimethoxyquinoline (7). To a suspension of compound **6** (100 mg, 0.373 mmol) in acetic acid (4 ml) and distilled water (2 ml) was added rapidly a solution of $TiCl_3$ (2 ml, 2.61 mmol, 13% in a 20% HCl solution). After stirring for 15 min at room temperature, a solution of 15 % NaOH was added until pH = 9. The reaction mixture was extracted with AcOEt, after the usual work-up a dark-yellow oil was obtained (80 mg, 90% yield). ^1H NMR (DMSO-d_6) 3.75 (3H, s), 3.85 (3H, s), 5.78 (NH_2, s), 6.71 (1H, s), 7.15 (1H, d, J = 5 Hz), 8.50 (1H, d, J = 5 Hz). IR ($CHCl_3$) 3327, 3287, 3030, 1634, 1604, 1458, 1277 cm^{-1}.

7-[5-(2,2-Dimethyl-4,6-dioxo-1,3-dioxanyliden)methylamino]-4-chloro-5,8-dimethoxyquinoline (8). A solution of Meldrum's acid (130 mg, 0.90 mmoles) in triethyl orthoformate (2 ml) was refluxed for 2 h. The solution obtained was added to compound **7** (200 mg, 0.82 mmoles) and the mixture was stirred until complete dissolution (about 5 min). After cooling to room temperature, a yellow precipitate was formed which was recrystallized in the ultrasound bath by adding methanol (5 ml). After filtration a pale yellow powder was obtained (260 mg, 80% yield). ^1H NMR ($CDCl_3$) 1.75 (6H, s), 3.95 (3H, s), 4.15 (3H, s), 6.82 (1H, s), 7.35 (1H, d, J = 5 Hz), 8.70 (1H, d, J = 5 Hz), 8.75 (1H, d, J = 12 Hz), 11.97 (NH, d, J = 12 Hz). ^{13}C NMR ($CDCl_3$) 27.4, 56.8, 62.9, 88.7, 94.4, 105.6, 117.9, 123.8, 130.5, 138.8, 142.2, 145.8, 150.4, 150.6, 154.1, 164.1, 165.4. IR ($CHCl_3$) 3010, 1740, 1620, 1571, 1275 cm^{-1}. Anal. Calcd for $C_{18}H_{17}N_2O_6Cl$: C, 55.03; H, 4.37; N, 7.13. Found : C, 55.5 ; H, 4.34; N, 7.07.

7-[5-(2,2-Dimethyl-4,6-dioxo-1,3-dioxanyliden)methylamino]-4-chloroquinoline-5,8-dione (9). To a solution of compound **8** (300 mg, 0.763 mmoles) in acetonitrile (5 ml) was added a solution of cerium ammonium nitrate (CAN) (1.83 g, 3.43 mmoles) in 2M sulfuric acid (6 ml). The mixture was stirred for 15 min at room temperature and then partitioned between a saturated NH_4Cl solution and dichloromethane. After the usual work-up an orange powder was obtained (200 mg, 73 % yield). ^1H NMR ($CDCl_3$) 1.75 (6H, s), 6.78 (1H, s), 7.72 (1H, d, J = 5 Hz), 8.50 (1H, d, J = 12 Hz), 8.88 (1H, d, J = 5 Hz), 11.97 (NH, d, J = 12 Hz). ^{13}C NMR ($CDCl_3$) 26.7, 92.6, 105.2, 115.5, 125.4, 131.1, 140.7, 142.5, 148.8, 151.4, 153.3, 161.5, 164.3, 177.0, 182.1. IR ($CHCl_3$) 3005, 1740, 1690, 1592, 1379, 1266 cm^{-1}. Anal. Calcd. for $C_{16}H_{11}N_2O_6Cl$: C, 52.97; H, 3.06; N, 7.72. Found : C, 52.22; H, 3.50; N, 7.40.

4-Chloro-(8*H*)-1,8-diazaanthracene-5,9,10-trione (10). A suspension of compound **9** (150 mg, 0.413 mmoles) in diphenylether (30 g) was refluxed under nitrogen for 15 min. After cooling to room temperature, petroleum ether (100 ml) was added. The mixture was filtered and the precipitate washed with petroleum ether. An orange powder was obtained (60 mg, 65% yield). ^{1}H NMR ($CDCl_3$) 7.20 (1H, d, J = 7 Hz), 7.72 (1H, d, J = 5 Hz), 8.75 (1H, d, J = 7 Hz), 8.85 (1H, d, J = 5 Hz), 12.1 (NH, bs). ^{13}C NMR ($CDCl_3$) 115.9, 117.6, 125.9, 131.1, 131.2, 145.8, 148.4, 150.3, 154.4, 156.1, 167.7, 178.2. IR ($CHCl_3$) 3056, 1707, 1599, 1561, 1382 cm^{-1}.

5,8-Dimethoxy-7-nitro-4-[(trifluoromethanesulfonyl)-oxy]quinoline (11). To a mixture of quinolinone **5** (0.25 g, 1 mmol), 2,6-dimethylpyridine (175 µl, 1.5 mmol), and 4-(dimethylamino)pyridine (12 mg, 0.1 mmol) in CH_2Cl_2 (10 ml), was added dropwise trifluoromethanesulfonic anhydride (175 µl, 1.05 mmol). After being stirred at room temperature for 1 h, the solution was partitioned between CH_2Cl_2 and a saturated NH_4Cl solution. After the usual work-up, purification of the crude product by flash column chromatography (CH_2Cl_2 : MeOH, 99 : 1) afforded a yellow solid, mp 105°C, (0.29 g, 76 % yield). ^{1}H NMR ($CDCl_3$) 4.02 (3H, s), 4.18 (3H, s), 7.20 (1H, s), 7.35 (lH, d, J = 5 Hz), 9.05 (1H, d, J = 5 Hz) , ^{13}C NMR ($CDCl_3$) 56.5, 64.5, 101.7, 116.4, 117.9, 118.9 [q, ^{1}J (^{13}C-^{19}F) = 320 Hz], 143.4, 144.3, 147.2, 150.6, 152.3, 153.3. IR (KBr) 3072, 1598, 1532 cm^{-1}. Anal. Calcd. for $C_{12}H_9F_3N_2O_7S$: C, 37.69 ; H, 2.36 ; N, 7.32. Found: C, 37.85 ; H, 2.61; N, 7.30.

5,8-Dimethoxy-7-nitro-4-[2'-(*tert*-butoxycarbonylamino)phenyl]quinoline (13). A mixture of triflate **11** (0.78 g, 2.03 mmol), stannane **7** (1.3 g, 3.65 mmol), lithium chloride (0.18 g, 4.25 mmol), copper (I) bromide (16 mg, 0.1 mmol) and tetrakis(triphenylphosphine)palladium(0) (120 mg, 0.1 mmol) in 1,4-dioxane (30 ml) was heated at 90 °C for 12 h under nitrogen. After cooling to room temperature, the reaction mixture was partitioned between AcOEt and a 5 % aqueous ethylenediamine solution (to remove the copper(I) salts from the crude product). After the usual work-up, purification of the crude product by flash column chromatography (hexane : AcOEt, 8 : 2) furnished a pale-yellow solid, mp 217°C, (0.8 g, 92 % yield). ^{1}H NMR ($CDCl_3$) 1.25 (9H, s), 3.45 (3H, s), 4.18 (3H, s), 5.94 (1H, s), 7.00 (1H, dd, J = 0.5 and 8.7 Hz), 7.02 (1H, s), 7.08 (1H, t, J = 8.9 Hz), 7.27 (1H, d, J = 4.5 Hz), 7.33 (1H, dd, J = 0.5 and 8.7 Hz), 7.8 (1H, d, J = 8.9 Hz), 8.91 (1H, d, J = 4.5 Hz). ^{13}C NMR ($CDCl_3$) 28.2, 56.1, 64.1, 80.5, 99.8, 121.2, 123.1, 126.0, 126.1, 128.2, 128.6, 132.3, 135.1, 142.3, 144.3, 144.7, 144.7, 150.9, 152.2, 152.9. IR (KBr) 3222, 3000, 2940, 1725, 1589, 1528, 1387 cm^{-1}. Anal. Calcd. for $C_{22}H_{23}N_3O_6$: C, 62.12 ; H, 5.42 ; N, 9.88. Found: C, 61.8 ; H, 5.76 ; N, 9.69.

7-Amino-5,8-dimethoxy-4-[2'-(*tert*-butoxycarbonylamino)phenyl]quinoline (14). A mixture of compound **13** (150 mg, 0.35 mmol), 10 % Pd/C catalyst (447 mg), absolute ethanol (10 ml) and cyclohexene (360 µl, 1.75 mmol) was refluxed for 45 min. After filtration, the filtrate was concentrated to yield a dark orange oil (130 mg, 94 % yield). ^{1}H NMR (DMSO-d_6) 1.30 (9H, s), 3.31 (3H, s), 3.82 (3H, s), 5.55 (2H, bs), 6.44 (1H, bs), 6.85 (1H, d, J = 5.3 Hz), 7.05 (1H, dd, J = 0.5 and 8.7 Hz), 7. 1 0 (1H, t, J = 8.8 Hz), 7.29 (1H,

dd, J = 0.5 and 8.7 Hz), 7.48 (1H, d, J = 8.8 Hz), 7.60 (1H, s), 8.61 (1H, d, J = 5.3 Hz). ^{13}C NMR ($CDCl_3$) 28.5, 56.2, 61.1, 80.8, 99.5, 114.1, 119.4, 120.8, 123.1, 128.3, 128.6, 130.4, 132.9, 135.1, 141.0, 143.1, 147.0, 147.1, 153.2, 153.8. IR (KBr) 3422, 3187, 2971, 1718, 1624, 1583, 1375 cm^{-1}. Anal. Calcd. for $C_{22}H_{25}O_4N_3$: C, 66.83 ; H, 6.33 ; N, 10.63. Found : C, 66.16 ; H, 6.32 ; N, 10.15.

7-[5-(2,2-Dimethyl-4,6-dioxo-1,3-dioxanyliden)methylamino]-5,8-dimethoxy-4-[2'-(*tert*-butoxycarbonylamino)phenyl]quinoline (15). A solution of Meldrum's acid (0.45 g, 3.12 mmol) in triethyl orthoformate (4.5 ml) was refluxed for 2 h and was added to amino derivative **14** (0.6 g, 1.52 mmol). The reaction mixture was refluxed for 15 min and evaporated. Purification of the crude product by flash column chromatography (hexane : AcOEt, 1 : 1) afforded a yellow solid, mp 203°C (0.76 g, 91 % yield). ^1H NMR ($CDCl_3$) 1.35 (9H, s), 1.80 (6H, s), 3.54 (3H, s), 4.27 (3H, s), 5.86 (1H, bs), 6.80 (1H, s), 7.08 (1H, d, J = 8.2 Hz), 7.14 (1H, t, J = 8.2 Hz), 7.22 (1H, d, J = 5.1 Hz), 7.40 (1H, t, J = 7.9 Hz), 7.95 (1H, d, J = 7.9 Hz), 9.02 (1H, d, J = 5.1 Hz), 9.78 (1H, d, J = 13.8 Hz), 12.11 (1H, d, J = 13.9 Hz) ^{13}C NMR ($CDCl_3$) 27.0, 27.1, 28.1, 56.2, 62.6, 80.5, 88.2, 93.3, 105.2, 118.2, 120.5, 122.8, 123.6, 128.1, 129.9, 132.4, 134.9, 138.5, 144.0, 150.0, 150.6, 152.9, 153.9, 163.7, 165.1. IR (KBr) 3431, 2980, 1723, 1678, 1619, 1583, 1380 cm^{-1}. Anal. Calcd. for $C_{29}H_{31}O_8N_3$: C, 63.38 ; H, 5.65 ; N, 7.65. Found : C, 63.32 ; H, 5.28 ; N, 7.44.

5-[5-(2,2-Dimethyl-4,6-dioxane-1,3-dioxanyliden)-methylamino]pyrido[2,3,4-kl]acridin-4-one (16). A solution of **15** (0.76 g, 1.38 mmol) in CH_3CN (10 ml) was treated with a solution of ammonium cerium(IV)nitrate (3.2 g, 6 mmol) in 2M H_2SO_4 (10 ml) at 23 °C. After stirring at room temperature for 30 min, the mixture was partitioned between AcOEt and an aqueous saturated NH_4Cl solution. After the usual work-up, the residue was chromatographed (CH_2Cl_2 : MeOH, 99 :1) to yield an orange solid (0.35 g, 63 % yield). ^1H NMR ($CDCl_3$) 1.73 (6H, s), 7.61 (1H, s), 7.82 (1H, td, J = 1.5 Hz and 8.3 Hz), 7.93 (1H, td, J = 1.5 and 8.3 Hz), 8.26 (1H, d, J = 8.3 Hz), 8.58 (1H, d, J = 8.3 Hz), 8.63 (1H, d, J = 5.3 Hz), 8.76 (1H, d, J = 13.8 Hz), 9.31 (1H, d, J = 5.3 Hz), 11.65 (1H, d, J = 13.8 Hz). ^{13}C NMR (DMSO-d_6) 27.1, 48.9, 78.2, 89.2, 105.0, 115.2, 121.2, 121.3, 124.1, 129.2, 130.9, 133.0, 136.8, 137.5, 145.1, 150.0, 150.1, 152.4, 162.4, 164.7, 177.5. IR ($CHCl_3$) 3681, 3010, 1688, 1591, 1470, 1384 cm^{-1}. Anal. Calcd. for $C_{22}H_{15}O_5N_3$: C, 65.83 ; H, 3.74 : N, 10.47. Found : C, 64.18 ; H, 4.18 ; N, 10.34. FABMS m/z 404 (M^++3H, 8), 403 (M^++2H, 4).

Meridine (12-hydroxy-benzo[*b*]pyrido[4,3,2-*de*][1,7]phenanthrolin-8-one) (1). A mixture of **16** (0.2 g, 0.5 mmol) in diphenylether (20 g) was refluxed under nitrogen for 5 min. After cooling to room temperature, petroleum ether (100 ml) was added. Filtration of the reaction mixture and concentration of the filtrate furnished a crude product which was purified by flash column chromatography (CH_2Cl_2 : MeOH, 95 : 5) to yield a solid, mp 255°C (0.11 g, 74 % yield). ^1H NMR ($CDCl_3$) 7.26 (1H, d, J = 5.4 Hz), 7.9 (1H, dd, J = 8 and 8 Hz), 8.00 (1H, dd, J = 8 and 8 Hz), 8.3 (1H, d, J = 7.9 Hz), 8.65 (1H, d, J = 5.4 Hz), 8.72 (1H, d, J = 5.6 Hz), 8.8 (1H, d, J = 5.4 Hz), 9.45 (1H, d, J = 5.6 Hz), 15.4 (OH, s). ^{13}C NMR ($CDCl_3$) 116.4, 117.0,

117.2, 119.7, 121.7, 123.3, 129.4, 129.6, 132.5, 138.0, 142.5, 147.6, 148.8, 151.6, 152.1, 153.7, 167.3, 180.3. IR (KBr) 3433, 3072, 1692, 1602, 1576, 1333 cm^{-1}. FABMS : m/z 302 (M^++3H, 100), 301 (M^++2H, 32). ESMS : m/z 621 (2M+Na^+), 338 (M+K^+), 322 (M+Na^+), 300 (M+H^+).

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