Tetrahedron Vol. 39, No 20, pp. 3261 to 3265, 1983
Printed in Great Britain

0040-4020/83 $3.00 + .00

STRUCTURE AND SYNTHESIS OF MENISPORPHINE, A NEW TYPE OF ISOQUINOLINE ALKALOID

ALKALOIDS OF *MENISPERMUM DAURICUM* DC. (9)[1]

J. KUNITOMO* and M. SATOH
Faculty of Pharmaceutical Sciences, Mukogawa Women's University, 4–16 Edagawa-cho, Nishinomiya 663, Japan

and

T. SHINGU
School of Pharmacy, Kobe-gakuin University, Arise Ikawadani-cho, Tarumi-ku, Kobe 673, Japan

(*Received in Japan* 11 *December* 1982)

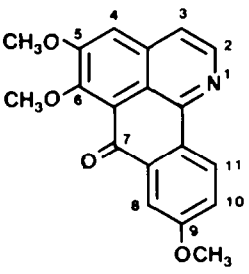
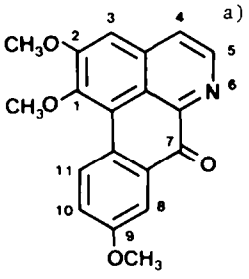
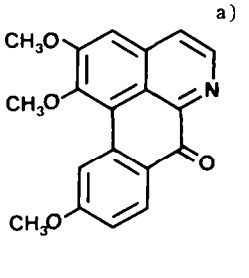
Abstract—The structure of an unknown yellow base from *Menispermum dauricum* DC. (Menispermaceae) was determined to be 5,6,9-trimethoxy-7*H*-dibenzo[*de*, *h*]quinolin-7-one from various spectral data and synthesis, and was named menisporphine. This is a new isoquinoline-type alkaloid having a 7H-dibenzo[*de*, *h*]quinolin-7-one skeleton for which the general term "oxoisoaporphine" is proposed.

The previous paper reported the isolation of six unknown yellow alkaloids together with three known isoquinoline alkaloids (cheilanthifoline, stepholidine and stepharine) from the rhizome of *Menispermum dauricum* DC. (Menispermaceae) collected in Kyoto, Japan.[1] This paper describes the characterization, structural establishment and synthesis of the tentatively named Base II reported in the previous paper. This yellow alkaloid was named menisporphine.

Menisporphine forms yellow needles from CH_2Cl_2–Me_2CO, m.p. 199.5–200.5°, and elemental analyses and MS established the formula as $C_{19}H_{15}NO_4$. Its IR spectrum (KBr) showed a conjugated CO band at 1660 cm^{-1}. The UV spectrum (Table) indicated a highly conjugated system similar to that of oxoaporphine-type alkaloids.[2,3] The MS data also supported this alkaloid type.[3] The ^1H NMR spectrum ($CDCl_3$) showed the presence of characteristic *ortho*-coupling protons at C_4-H and C_3-H [δ 7.55 (1H, d, J = 5.5Hz), 8.65 (1H, d, J = 5.5 Hz)] of isoquinoline skeleton and four aromatic protons with three OMe groups. Based on these data, the structure of 1,2,9- or 1,2,10-trimethoxyoxoaporphine (**1** or **2**)[4] was predicted, but neither seemed to be correct as can be seen from the Table. The possible structure for menisporphine according to several pieces of spectral data was assumed to be that of trimethoxy-7*H*-dibenzo[*de*, *h*]quinolin-7-one which is related to the isomer of trimethoxyoxoaporphine-type alkaloids. In order to determine the position of the three OMe groups, the NOE and internuclear double resonance (INDOR) were used. In the INDOR experiments of this alkaloid, the signal of the aromatic proton at δ 7.40 was observed as a singlet upon irradiation at the frequency of aromatic proton at C_4-H (δ 7.55) of the isoquinoline skeleton. Furthermore, the NOE effect was also detected, i.e. irradiation at the frequency of C_3-H (δ 7.55) in menisporphine enhanced by *ca* 10% the peak area of the C_4-H signal (δ 7.40). Consequently, the signal of the aromatic proton as a singlet at δ 7.40 was assigned to the C_4-H of the 7*H*-dibenzo[*de*, *h*]quinolin-7-one skeleton, and the positions of two of the three OMe groups were determined to be at C-5 and C-6 of this skeleton. The third OMe group was found to be at C-9 or C-10 according to the AMX type splitting and the coupling constant of the signals of the residual three aromatic protons in the ^1H NMR spectrum. The proton at C_{11}-H in this type of skeleton is found appreciably downfield due to ring current effect of aromatized isoquinoline ring similarly as C_{11}-H in benzanthrone derivatives[5] or oxoaporphine-type alkaloids. The signals of *ortho*-aromatic protons at δ 7.33 and δ 8.79 were assigned to C_{10}-H and C_{11}-H, respectively. The position of the remaining OMe group must be C-9. These results suggested that menisporphine would be 5,6,9-trimethoxy-7*H*-dibenzo[*de*, *h*]quinolin-7-one (**3**).

Final evidence for this structure came from its synthesis. Many compounds having the 7*H*-dibenzo[*de*, *h*]quinolin-7-one skeleton are used as dyes and can be synthesized by various methods, but the positions of the substituent groups are still uncertain.[6] The desired compound (**3**) was synthesized as shown in Chart 1. The starting material, N(3′, 4′, β-trimethoxyphenethyl)-2-bromo-4-methoxybenzamide (**6a**), was obtained by the Schotten-Baumann reaction of 3,4,β-trimethoxyphenethylamine and 2-bromo-4-methoxybenzoyl chloride (**5a**). The Bischler-Napieralski reaction of this benzamide derivative (**6a**) with phosphorus oxychloride afforded 1-(2′-bromo-4′-methoxyphenyl)-6,7-dimethoxyisoquinoline (**7a**). This compound (**7a**) on reaction with cuprous cyanide gave the corresponding cyano-derivative (**8a**) in high yield. The cyano compound (**8a**) was hydrolyzed to afford the corresponding carboxylic acid (**9a**), which is soluble in water. Confirmation of **9a** was carried out by the formation of its methyl ester. The second ring cyclization of the **9a** with polyphosphoric acid afforded 6-hydroxy-5,9-dimethoxy-7*H*-dibenzo[*de*, *h*]quinolin-7-one (**10a**) which demethylated the OMe group at C-6. Treatment of this compound (**10a**) with methyl iodide in the presence of silver oxide produced the desired compound (**3**) as yellow needles,

Table 1. The data of menisporphine and trimethoxyoxoaporphine

		 menisporphine (**3**)	 (**1**)	 (**2**)
mp (°C)		199.5-200.5	201-203	200-201
Anal [b]		$C_{19}H_{15}NO_4$		
UV λ_{max}^{EtOH} (log ε)		254, 288 sh, 310 sh, 319, 334 sh, 368, 420 (4.72, 4.13, 3.96, 3.97, 3.94, 3.91, 3.97)	244, 271, 292 sh, 377, 444 (4.46, 4.44, 4.16, 3.68, 3.62)	242, 272, 284 sh, 312, 351, 387 (4.45, 4.44, 4.19, 3.84, 4.07, 4.00)
IR ν_{max}^{KBr}		1660 cm^{-1}	1680 cm^{-1}	1665 cm^{-1}
^1H NMR ($CDCl_3$) δ: (*J*: Hz)	OCH_3	3.98, 4.08, 4.15	3.98, 3.98, 4.03	3.96, 3.99, 4.03
	arom. H	7.33(d.d, *J* =2.5, 9.0), 7.40(s), 7.55(d, *J* =5.5), 7.86(d, *J* =2.5), 8.65(d, *J* =5.5), 8.79(d, *J* =9.0)	7.19(s, C_3-H), 7.28(d.d, *J* =3.0, 9.0, C_{10}-H), 7.72(d, *J* =6.0, C_4-H), 8.01(d, *J* =3.0, C_8-H), 8.81(d, *J* =6.0, C_5-H), 8.99(d, *J* =9.0, C_{11}-H)	7.03(d.d, *J* =3.0, 9.0, C_9-H), 7.08(s, C_3-H), 7.62(d, *J* =6.0, C_4-H), 8.48(d, *J* =9.0, C_8-H), 8.63(d, *J* =3.0, C_{11}-H) 8.77(d, *J* =6.0, C_5-H)
MS (*m/e*)		321(M^+, base peak), 306, 293, 278, 261	321(M^+), 320(base peak), 306, 305, 278	321(M^+, base peak), 306, 278, 263

a) These data cited from reference 4.

b) Menisporphine (**3**): Anal. Calcd: C, 71.02; H, 4.71; N, 4.36.
Found: C, 71.10; H, 4.63; N, 4.44

m.p. 199–200°. It was identified by direct comparison of its spectra, (UV, IR, ^1H NMR and MS) and TLC with those of natural product, menisporphine. From the reaction product of 0-methylation, the corresponding enol ether (**11**), which is related to the isomer of compound **3** was also obtained in low yield.

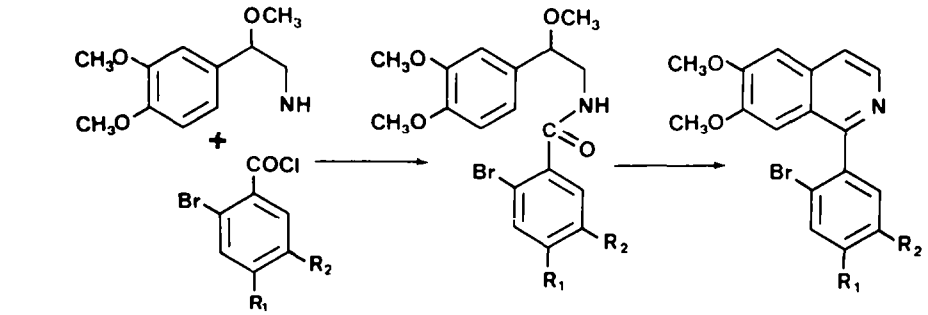
This isoquinoline-type alkaloid has an entirely new skeleton (7*H*-dibenzo[*de*, *h*]quinolin-7-one) and we propose to name it "oxoisoaporphine" because of its relationship to the isomer oxoaporphine. Biogenesis for oxoisoaporphine-type alkaloids in plants probably is as Chart 2.

The precursor seemed to be a papaverinol derivative. The biogenetic route may involve the formation of isoquinoline derivative containing a cyclobutane ring from the precursor by intramolecular oxidative coupling, followed by a dienone enol rearrangement with fission of the cyclobutane ring. Finally, electrophilic substitution to the aromatic ring of the aldehyde leads to this new skeleton ring.

5,6,10-Trimethoxy-7*H*-dibenzo[*de*, *h*]quinolin-7-one (**4**), which is an isomer of menisporphine (**3**), was also synthesized by the same method and the desired **4** was obtained as pale yellow needles, m.p. 195–196°. In the ^1H NMR ($CDCl_3$) of **4**, the signal of aromatic proton at C_{11}–H (δ 8.35) is present somewhat upfield than that at C_8–H (δ 8.37). Oppositely, the signal of aromatic proton at C_{11}–H (δ 8.79) of menisporphine (**3**) shifts appreciably downfield in the comparison with that at C_8–H (δ 7.86). The reason for this fact seems to be due to the positional difference of the OMe substituents (C_9- or C_{10}-position) of both **3** and **4**, as a similar relationship between the signals of the aromatic protons of C_8–H and C_{11}–H in the trimethoxyoxoaporphines **1** and **2** was observed.

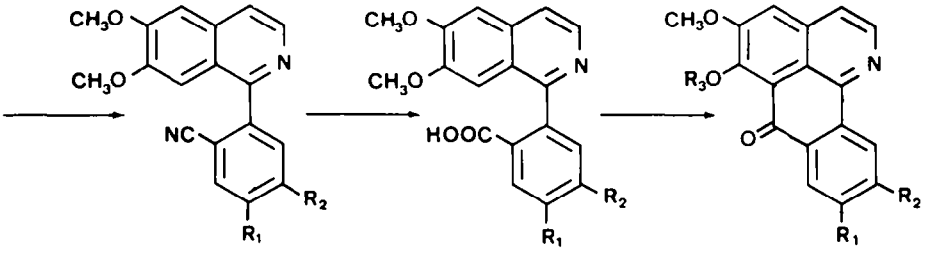
EXPERIMENTAL

All m.ps are uncorrected. ^1H NMR spectra were recorded on a JNM-FX 200 spectrometer in $CDCl_3$ with TMS as an internal standard. MS spectra were recorded on a direct inlet system at 70 eV using a Hitachi RMU-6 spectrometer. All organic solutions were dried over $MgSO_4$.



(**5a**) R_1=OCH_3, R_2=H (**6a**) R_1=OCH_3, R_2=H (**7a**) R_1=OCH_3, R_2=H

(**5b**) R_1=H, R_2=OCH_3 (**6b**) R_1=H, R_2=OCH_3 (**7b**) R_1=H, R_2=OCH_3

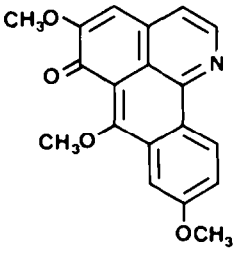


(**8a**) R_1=OCH_3, R_2=H (**9a**) R_1=OCH_3, R_2=H (**10a**) R_1=OCH_3, R_2=R_3=H

(**8b**) R_1=H, R_2=OCH_3 (**9b**) R_1=H, R_2=OCH_3 (**10b**) R_1=R_3=H, R_2=OCH_3

(**3**) R_1=OCH_3, R_2=H, R_3=CH_3

(**4**) R_1=H, R_2=OCH_3, R_3=CH_3



(**11**)

Chart 1.

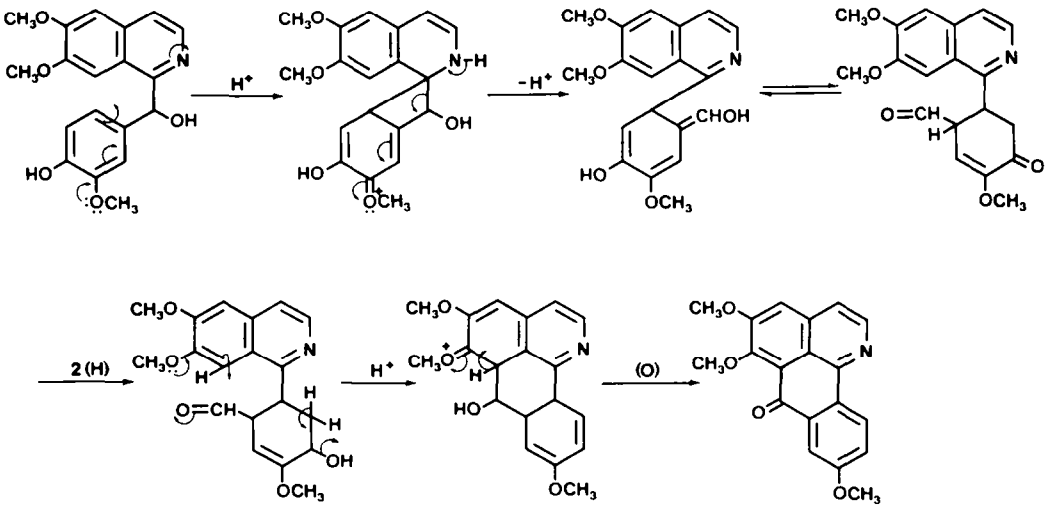


Chart 2. The biogenetic route of oxoisoaporphine-type alkaloid.

(a) *Synthesis of* 5,6,9-*trimethoxy*-7H-*dibenzo*[de, h]*quinolin*-7-*one* (**3**)

N-(3', 4', *β*-*Trimethoxyphenethyl*)-2-*bromo*-4-*methoxybenzamide* (**6a**). To a soln of 3,4,*β*-trimethoxyphenethylamine (14.21 g) in 300 ml Et_2O and 480 ml of 10% NaOHaq, **5a** was added dropwise with stirring at 0–5° in anhyd. Et_2O. Compound **5a** was formed from 2-bromo-4-methoxybenzoic acid[7] (15.5 g) and excess $SOCl_2$ in the usual way. Stirring was continued for 1 hr. The ppt was filtered off and dissolved in CH_2Cl_2. The CH_2Cl_2 layer was washed with 10% HClaq and water, and dried. Removal of the solvent by evaporation and recrystallization from Et_2O·MeOH gave **6a** (25.92 g, 91.2%) as colorless needles, m.p. 114–116°. UV λ_{max}^{EtOH} nm (log ϵ): 232 (4.23), 279 (3.64), 289 (3.53). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1655, 3450. ^1H NMR δ: 3.28, 3.83, 3.89, 3.90 (3H × 4, each s, OCH_3 × 4), 3.38, 3.90 (2H, C_α–H × 2), 4.34 (1H, d.d, J = 4.0, 9.0 Hz, C_β–H), 6.52 (1H, s, NH), 6.86 (1H, d.d, J = 2.5, 8.5 Hz, C_5–H), 6.89 (3H, C_2–H, C_5–H and C_6–H), 7.12 (1H, d, J = 2.5Hz, C_3–H), 7.56 (1H, d, J = 8.5Hz, C_6–H). MS *m*/*z* (%): 425 (1.6), 423 (M^+, 1.6), 215 (3.1), 213 ($(CH_3O{\cdot}BrC_6H_3CO^+$, 3.1), 195 ($((CH_3O)_2C_6H_3CH(OCH_3)CH_2^+$, 4.7), 194 (38.8), 182 (13.4), 181 ($((CH_3O)_2C_6H_3CHOCH_3^+$, base peak), 166 (181–$CH_3$, 6.5). (Found; C, 53.62; H, 5.26; N, 3.07. Calc for $C_{19}H_{22}BrNO_5$: C, 53.82; H, 5.23; N, 3.30%).

1-(2'-*Bromo*-4'-*methoxyphenyl*)-6,7-*dimethoxyisoquinoline* (**7a**). Compound **6a** (2.12 g) was heated with $POCl_3$ (9 ml) and anhyd toluene (15 ml) at 120° for 2.5 hr. The solvent and the excess reagent were removed by evaporation *in vacuo*, and residual reagent was decomposed by adding MeOH and 5% HClaq. The acidic soln was washed once with Et_2O, make alkaline with 10% NH_4OHaq and extracted with CH_2Cl_2. The extract was washed with H_2O, dried and the solvent was evaporated. The residue was purified by column chromatography on silica gel (eluted by Et_2O). Recrystallization from MeOH gave 1.21 g (64.7%) of **7a** as colorless plates, m.p. 123–124°; UV λ_{max}^{EtOH} nm (log ϵ): 243 (4.69), 281 (sh, 3.77), 287 (sh, 3.70), 316 (sh, 3.49), 329.5 (3.61). ^1H NMR δ: 3.83, 3.89, 4.05 (3H × 3, each s, OCH_3 × 3), 6.87 (1H, s, C_5-H), 7.01 (1H, d.d, J = 2.5, 8.5Hz, C_5–H), 7.13 (1H, s, C_8–H), 7.27 (1H, d, J = 2.5Hz, C_3–H), 7.38 (1H, d, J = 8.5Hz, C_6–H), 7.55 (1H, d, J = 5.5Hz, C_4–H), 8.48 (1H, d, J = 5.5Hz, C_3-H). MS *m*/*z* (%): 375 (79.5), 373 (M^+, 79.5), 360 (375–CH_3, 20.5), 358 (M^+–CH_3, 21.4), 294 (M^+-Br, base peak), 279 (294–CH_3, 18.8), 278 (16.1), 250 (278–CO, 20.5), 236 (250–CH_2, 20.5). (Found: C, 57.86; H, 4.30; Calc for $C_{18}H_{16}BrNO_3$: C, 57.77; H, 4.31; N, 3.74%).

1-(2'-*Cyano*-4'-*methoxyphenyl*)-6,7-*dimethoxyisoquinoline* (**8a**). Compound **7a** (2.17 g) was heated with cuprous cyanide (772 mg) in 25 ml DMF at 180° for 5 hr. The mixture was poured into 50 ml ice water, made alkaline with 10% NH_4OHaq and extracted with CH_2Cl_2. The extract was thoroughly washed with H_2O and dried. Recrystallization from Me_2CO gave 1.53 g (82.4%) of **8a** as colorless needle, m.p. 158–158.5°. UV λ_{Max}^{EtOH} nm (log ϵ): 241 (4.73), 332 (3.85). IR $\nu_{max}^{CHCl_3}$: 2250 cm^{-1} (CN). ^1H NMR δ: 3.86, 3.93, 4.05 (3H × 3, each s, OCH_3 × 3), 6.99, 7.15 (1H × 2, each s, C_5–H and C_8–H), 7.26 (1H, d.d, J = 3.0, 9.0Hz, C_5–H), 7.35 (1H, d, J = 3.0Hz, C_3–H), 7.57 (1H, d, J = 5.5Hz, C_4–H), 7.60 (1H, d, J = 9.0Hz, C_6–H), 8.51 (1H, d, J = 5.5Hz, C_3–H). MS *m*/*z* (%): 321 (M^+ + 1, 24.3), 320 (M^+, base peak), 319 (M^+–1, 20.9), 305 (M^+–CH_3, 25.2), 290 (305–CH_3, 34.8), 262 (290-CO, 12.2). (Found: C, 71.37; H, 4.93; N, 8.80. Calc. for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.75%).

1-(2'-*Carboxy*-4'-*methoxyphenyl*)-6,7-*dimethoxyisoquinoline* (**9a**). The above **8a** (2.55g) was heated under reflux with 40% KOHaq (60 ml) and diethylene glycol (40 ml) until the evolution of NH_3 gas ceased (24 hr). The mixture was poured into water, and washed with Et_2O. The alkaline soln was neutralized to pH 7 with AcOH, extracted three times with BuOH, and the solvent was evaporated *in vacuo*. The residual crude product was recrystallized from MeOH to give 1.10 g (40.7%) of **9a** as colorless needles, m.p. 253–254°. UV λ_{max}^{EtOH} nm (log ϵ): 242 (4.81), 318 (sh, 3.92), 330 (3.97). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1600 (COO^-). ^1H NMR δ: 3.72, 3.77, 3.84 (3H × 3, each s, OCH_3 × 3), 7.29 (1H, s, C_5–H), 7.31 (1H, d.d, J = 3.0, 9.0 Hz, C_5–H), 7.50 (1H, s, C_8–H), 7.66 (1H, d, J = 5.5 Hz, C_4–H), 7.77 (1H, d, J = 9.0 Hz, C_6–H), 8.05 (1H, d, J = 3.0Hz, C_3–H), 8.71 (1H, d, J = 5.5 Hz, C_3–H). MS *m*/*z* (%): 339 (M^+, 5.2), 322 (M^+–OH, 56.5), 295 (79.3), 294 (322-CO, 55.9), 280 (295-CH_3, base peak). (Found: C, 66.79; H, 5.31; N, 3.85. Calc for $C_{19}H_{17}NO_5.1/4H_2O$: C, 66.37; H, 5.13: N, 4.07%).

Methyl ester of **9a**. Compound **9a** (0.5 g) in MeOH (10 ml) was treated with excess ethereal CH_2N_2 and kept at room temp overnight. After treatment in the usual way, the desired product was recrystallized from EtOAc and petroleum ether to give colorless needles, m.p. 122–123°. UV λ_{max}^{EtOH} nm (log ϵ): 240 (4.69), 330 (3.52). IR $\nu_{max}^{CHCl_3}$: 1720 cm^{-1} ($COOCH_3$). ^1H NMR δ: 3.41, 3.80, 3.94, 4.04 (3H × 4, each s, OCH_3 × 4), 6.91 (1H, s, C_5–H), 7.12 (1H, s, C_8–H), 7.19 (1H, d.d, J = 3.0, 8.5Hz, C_5–H), 7.48 (1H, d, J = 8.5Hz, C_6–H), 7.50 (1H, d, J = 5.5Hz, C_4–H), 7.57 (1H, d, J = 3.0Hz, C_3–H), 8.43 (1H, d, J = 5.5 Hz, C_3–H). MS *m*/*z* (%): 354 (M^+ + 1, 23.0), 353 (M^+, 93.2), 322 (M^+–OCH_3, base peak), 294 (322–CO, 9.2). (Found: C, 67.39; H, 5.39; N, 3.78. Calc for $C_{20}H_{19}NO_5$: ,C, 67.98; H, 5.42; N, 3.96%).

6-*Hydroxy*-5,9-*dimethoxy*-7H-*dibenzo*[de, h]*quinolin*-7-*one* (**10a**). the above **9a** (1.0 g) was heated with polyphosphoric acid (25 ml) at 100° for 1 hr with stirring. The mixture was poured into ice water, made alkaline with 10% NH_4OHaq and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried. Recrystallization from CH_2Cl_2 gave 0.63 g (69.5%) of a product as yellow needles, m.p. 248–249°. UV λ_{max}^{EtOH} nm (log ϵ) 238 (sh, 4.38), 254 (4.62), 292 (sh, 3.76), 307 (3.53), 319 (3.44), 358 (sh, 3.77), 366 (3.79), 406 (sh, 3.51), 430 (3.83), 455 (3.84). This spectrum shifts to bathochromic by addition of 10% NaOH soln or 10% HCl soln. ^1H NMR δ: 4.02, 4.10 (3H × 2, each s, OCH_3 × 2), 5.94 (1H, s, OH), 7.29 (1H, s, C_4–H), 7.45 (1H, d.d, J = 3.0, 9.0Hz, C_{10}–H), 7.58 (1H, d, J = 5.0Hz, C_3–H), 7.92 (1H, d, J = 3.0Hz, C_8–H), 8.74 (1H, d, J = 5.0Hz, C_2–H), 8.95 (1H, d, J = 9.0Hz, C_{11}–H). MS *m*/*z* (%): 308 (M^+ + 1, 33.3), 307 (M^+, base peak), 278 (M^+–CO, 32.3). (Found: C, 70.14; H, 4.15; N, 4.49. Calc for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56%).

O-*Methylation of phenolic base* **10a** *with methyl iodide in the presence of silver oxide*. The base **10a** (246 mg) in MeOH (6.0 ml) and $CHCl_3$ (8.0 ml) were heated under reflux with Ag_2O (1.3 g) and MeI (12.0 ml) at 60° for 6 hr with stirring. The mixture was filtered, and the ppt was thoroughly washed with $CHCl_3$. The $CHCl_3$ layer was washed with H_2O and dried. The residue was purified by column chromatography on silica gel (eluted by CH_2Cl_2 containing 1% Me_2CO) to give crystallised **3** and **11**. 5,6,9-*Trimethoxy*-7H-*dibenzo*[de, h]*quinolin*-7-*one* (**3**) as yellow needles, m.p. 199–200° (41.5% yield). UV λ_{max}^{EtOH} nm (log ϵ): 254 (4.45), 290 (sh, 4.44), 320 (3.75), 368 (3.68), 420 (3.78). $\lambda_{max}^{10\%HCl\text{-}EtOH}$ nm (log ϵ): 270 (4.43), 300 (sh, 3.81), 320 (sh, 3.69), 332 (3.69), 428 (3.70). IR ν_{max}^{KBr}: 1660 cm^{-1}. ^1H NMR δ: 3.99, 4.08, 4.17 (3H × 3, each s, OCH_3 × 3), 7.34 (1H, d.d, J = 2.5, 9.0Hz, C_{10}–H), 7.38 (1H, s, C_4–H), 7.55 (1H, d, J = 5.5Hz, C_3–H), 7.89 (1H, d, J = 2.5Hz, C_8–H), 8.66 (1H, d, J = 5.5Hz, C_2–H), 8.80 (1H, d, J = 9.0Hz, C_{11}–H). MS *m*/*z* (%): 321 (M^+, base peak), 306 (M^+–CH_3, 30.0), 292 (M^+–1–CO, 64.0), 278 (M^+–CO–CH_3, 17.7), 261 (12.5). (Found: C, 71.00; H, 4.64; N, 4.15. Calc for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36%). This compound was identified by direct comparison (UV, IR, ^1H NMR, MS, TLC and mixed m.p.) with natural menisporphine. 5,7,9-*Trimethoxy*-6H-*dibenzo*[de, h]*quinolin*-6-*one* (**11**), yellow needles, m.p. 173–175° (20.3% yield). UV λ_{max}^{EtOH} nm (log ϵ): 241 (4.60), 281 (sh, 4.12), 287 (4.13), 362 (3.93), 398 (sh, 3.88), 448 (sh, 3.65). $\lambda_{max}^{10\%HCl\ EtOH}$ nm (log ϵ): 245 (4.54), 289 (sh, 4.08), 299 (4.10), 317 (sh, 3.97), 374 (sh, 3.94), 392 (3.97), 430 (3.83), 450 (3.83). IR $\nu_{max}^{CHCl_3}$: 1645 cm^{-1}. ^1H NMR δ: 4.00, 4.03, 4.23 (3H × 3, each s, OCH_3 × 3), 6.80 (1H, s, C_4–H), 7.47 (1H, d, J = 5.0Hz, C_3–H), 7.52 (1H, d.d, J = 2.5, 9.0Hz, C_{10}–H), 7.89 (1H, d, J = 2.5Hz, C_8–H), 8.90 (1H, d, J = 5.0Hz, C_2–H), 9.22 (1H, d, J = 9.0Hz, C_{11}–H). MS *m*/*z* (%): 321 (M^+, base peak), 306 (M^+–CH_3, 42.7), 292 (M^+–1–CO, 32.2), 277 (18.2), 261 (16.9), 235 (10.6). (Found: C, 66.95; H, 4.62; N, 3.81. Calc for $C_{19}H_{15}NO_4{\cdot}H_2O$: C, 67.25; H, 5.05; N, 4.13%).

(b) *Synthesis of* 5,6,10-*trimethoxy*-7H-*dibenzo*[de, h]*quinolin*-7-*one* (**4**)

N-(3',4',*β*-*Trimethoxyphenethyl*)-2-*bromo*-5-*methoxybenzamide* (**6b**), recrystallization from Et_2O.MeOH as colorless plates, m.p. 93–94° (81.9% yield). UV λ_{max}^{EtOH} nm (log ϵ): 210.5 (4.56), 231.5 (4.33), 284 (3.69). IR ν_{max}^{KBr} cm^{-1}: 3325 (NH), 1665 (NHC=O). ^1H

NMR δ: 2.06 (1H, s, NH), 3.30, 3.79, 3.90 (3H × 4, each s, OCH_3 × 4), 3.42 (2H, s, CH_2), 4.40 (1H, q, β-H), 6.81 (1H, d.d, J = 3.0, 9.0 Hz, C_4–H), 6.93 (3H, each s, C_2–H, C_5–H and C_6–H), 7.08 (1H, d, J = 3.0 Hz, C_6–H), 7.47 (1H, d, J = 9.0 Hz, C_3–H). MS m/z (%): 425 (5.5), 423 (M^+, 5.7), 215 (2.4), 213 ($CH_3O{\cdot}BrC_6H_3CO^+$, 2.6), 195 ($(CH_3O)_2C_6H_3CH(OCH_3)CH_2^+$, 8.6), 194 (67.5), 182 (30.0), 181 ($(CH_3O)_2C_6H_3CHOCH_3^+$, base peak), 179 (1.0). (Found: C, 52.64; H, 5.50; N, 2.96. Calc for $C_{19}H_{22}BrNO_5{\cdot}1/2H_2O$: C, 52.67; H, 5.35; N, 3.23%).

1-(2′-*Bromo*-5′-*methoxyphenyl*)-6,7-*dimethoxyisoquinoline* (**7b**), pale yellow oily compound (54.2% yield) which showed a single spot on TLC when it was purified by column chromatography on silica gel (eluted by CH_2Cl_2 solvent). UV λ_{max}^{EtOH} nm (log ϵ): 242 (4.75), 287 (3.74), 317.5 (3.60), 330.5 (3.62). ^{1}H NMR δ: 3.82, 3.83, 4.03 (3H × 3, each s, OCH_3 × 3), 6.83 (1H, d.d, J = 1.0, 3.0Hz, C_6–H), 6.95 (1H, d.d, J = 3.0, 9.0Hz, C_4–H), 7.02 (1H, s, C_5–H), 7.13 (1H, s, C_8–H), 7.56 (1H, d, J = 5.5Hz, C_4–H), 7.59 (1H, d.d, J = 1.0, 9.0Hz, C_3–H), 8.50 (1H, d, J = 5.5Hz, C_3–H). MS m/z (%): 375 (73.5), 373 (M^+, 73.9), 295 (32.5), 294 (M^+–Br, base peak).

1-(2′-*Cyano*-5′-*methoxyphenyl*)-6,7-*dimethoxyisoquinoline* (**8b**), colorless plates (70.9% yield), m.p. 147–149° (from Me_2CO). UV λ_{max}^{EtOH} nm (log ϵ): 210 (4.28), 243 (4.66), 319 (sh, 3.55), 332 (3.61). IR ν_{max}^{KBr}: 2230 cm^{-1} (CN). ^{1}H NMR δ: 3.86, 3.88, 4.01 (3H × 3, each s, OCH_3 × 3), 7.02, 7.16 (1H × 2, each s, C_5–H and C_8–H), 7.06 (1H, d.d, J = 3.0, 9.0Hz, C_4–H), 7.18 (1H, d, J = 3.0Hz, C_6–H), 7.57 (1H, d, J = 5.5Hz, C_4–H), 7.78 (1H, d, J = 9.0Hz, C_3–H), 8.52 (1H, d, J = 5.5Hz, C_3–H). MS m/z (%): 321 (46.9), 320 (M^+, base peak), 319 (29.3), 305 (M^+–CH_3, 40.6), 290 (14.3), 289 (22.3). (Found: C, 71.04; H, 4.92; N, 8.46. Calc for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.75%).

1-(2′-*Carboxy*-5′-*methoxyphenyl*)-6,7-*dimethoxyisoquinoline* (**9b**), colorless needles (41.1% yield), m.p. 201–203.5° (from MeOH). UV λ_{max}^{MeOH} nm (log ϵ): 241 (4.77), 316 (3.72), 328 (3.75). IR ν_{max}^{KBr}: 1710 cm^{-1} (COOH). ^{1}H NMR δ: 3.68, 3.78, 3.88 (3H × 3, each s, OCH_3 × 3), 7.18 (1H, d.d, J = 3.0, 9.0Hz, C_4–H), 7.30, 7.38 (1H × 2, each s, C_5–H and C_8–H), 7.38 (1H, d, J = 3.0Hz, C_6–H), 7.68 (1H, d, J = 5.5Hz, C_4–H), 8.50 (1H, d, J = 9.0Hz, C_3–H), 8.71 (1H, d, J = 5.5Hz, C_3–H). MS m/z (%): 339 (M^+, 19.0), 322 (M^+–OH, 20.0), 295 (M^+–CO_2, 87.1), 294 (M^+–COOH, 61.7), 281 (295–CH_3, 22.3), 280 (294–CH_3, base peak), 265 (24.5), 264 (64.2). (Found: C, 66.08; H, 4.89; N, 3.96. Calc for $C_{19}H_{17}NO_5{\cdot}1/3H_2O$: C, 66.07; H, 5.15; N, 4.05%). *Methyl ester of* **9b**, colorless needles, m.p. 117–120° (from Et_2O-Me_2CO). UV λ_{max}^{EtOH} nm (log ϵ): 239 (4.36), 315 (3.37), 328 (3.36). IR $\nu_{max}^{CHCl_3}$: 1705 cm^{-1} ($COOCH_3$). ^{1}H NMR δ: 3.41, 3.77, 3.88, 4.03 (3H × 4, each s, OCH_3 × 4), 6.84, 7.12 (1H × 2 each s, C_5–H and C_8–H), 7.01 (1H, d, J = 2.5Hz, C_6–H), 7.05 (1H, d.d, J = 2.5, 9.0Hz, C_4–H), 7.52 (1H, d, J = 5.5Hz, C_4–H), 8.21 (1H, d, J = 9.0Hz, C_3–H), 8.44 (1H, d, J = 5.5Hz, C_3–H). MS m/z (%): 354 (M^+ + 1, 16.3), 353 (M^+, 63.8), 323 (354–OCH_3, 22.9), 322 (M^+–OCH_3, base peak), 294 (322–CO, 9.5), 280 (14.1). (Found: C, 67.74; H, 5.41; N, 3.74. Calc for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96).

6-*Hydroxy*-5,10-*dimethoxy*-7H-*dibenzo*[de, h]*quinolin*-7-*one* (**10b**), yellow needles (64.1% yield), m.p. 244–245° (from CH_2Cl_2). UV λ_{max}^{EtOH} nm (log ϵ): 219 (4.52), 252 (4.50), 310 (3.73), 346 (3.98), 380 (3.87), 402 (3.97), 422 (4.04) (bathochromic shifts upon addition of alkali). ^{1}H NMR δ: 4.10 (6H, s, OCH_3 × 2), 7.22 (1H, d.d, J = 3.0, 9.0Hz, C_9–H), 7.23 (1H, s, C_4–H), 7.60 (1H, d, J = 5.5Hz, C_3–H), 8.43 (1H, d, J = 9.0Hz, C_8–H), 8.48 (1H, d, J = 3.0Hz, C_{11}–H), 8.73 (1H, d, J = 5.5Hz, C_2–H). MS m/z (%): 307 (M^+, base peak), 306 (M^+–1, 31.4), 278 (M^+–CO, 38.8), 261 (26.2). (Found: C, 70.48; H, 4.19; N, 4.61. Calc for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56%).

5, 6, 10-*Trimethoxy*-7H-*dibenzo*[de, h]*quinolin*-7-*one* (**4**), pale yellow needles (67.0% yield), m.p. 195–196° (from Me_2CO-CH_2Cl_2 mixted solvent). UV λ_{max}^{EtOH} nm (log ϵ): 217 (4.66), 254 (4.46), 262 (4.46), 270 (sh, 4.43), 280 (sh, 4.25), 302 (sh, 3.85), 315 (3.93), 346 (4.13), 376 (4.05). IR ν_{max}^{KBr}: 1655 cm^{-1} (C=O). ^{1}H NMR δ: 4.05, 4.07, 4.15 (3H × 3, each s, OCH_3 × 3), 7.15 (1H, d.d, J = 3.0, 9.0 Hz, C_9–H), 7.35 (1H, s, C_4–H), 7.58 (1H, d, J = 5.5Hz, C_3–H), 8.35 (1H, d, J = 3.0Hz, C_{11}–H), 8.37 (1H, d, J = 9.0Hz, C_8–H), 8.67 (1H, d, J = 5.5Hz, C_2–H). MS m/z (%): 321 (M^+, base peak), 306 (M^+–CH_3, 32.0), 292 (35.0). (Found: C, 70.90; H, 4.56; N, 4.20. Calc for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36%).

Acknowledgement—The authors are grateful to Miss K. Suwz, Mukogawa Women's University, for elemental analyses and measurements of UV, IR, ^{1}H NMR and MS.

REFERENCES

[1]Part 8. Y. Okamoto, S. Tanaka, K. Kitayama, M. Isomoto, M. Masaishi, H. Yanagawa and J. Kunitomo, *Yakugaku Zasshi* **91**, 684 (1971). This paper constitutes Part 279 in the series *Studies on the Alkaloids of Menispermaceous Plants* (Part 278, see S. Kondo, M. Matsui and Y. Watanabe, *Chem. Pharm. Bull. Tokyo* in press (1983). Part of the contents was reported by rapid publication in J. Kunitomo and M. Satoh, *Chem. Pharm. Bull Tokyo* **30**, 2659 (1982).

[2]M. Shamma, *The Isoquinoline Alkaloids*, p. 245. Academic Press, New York (1972).

[3]R. H. F. Manske, *The Alkaloids*, XIV, p. 225. Academic Press, New York (1973).

[4]J. Kunitomo, Y. Murakami and M. Sugisakon, *Yakugaku Zasshi* **99**, 102 (1979).

[5]A. Vaidyanathan, *Ind. J. Chem.* **21B**, 356 (1982).

[6]C. F. H. Allen, *6-Membered Heterocyclic Nitrogen Compounds with Four Condensed Rings*, p. 204. Interscience, New York (1951).

[7]M. Tomita and K Fujitani, *Yakugaku Zasshi* **76**, 1126 (1956).