FURTHER EVIDENCE FOR THE STRUCTURE OF BIANFUGECINE[1]

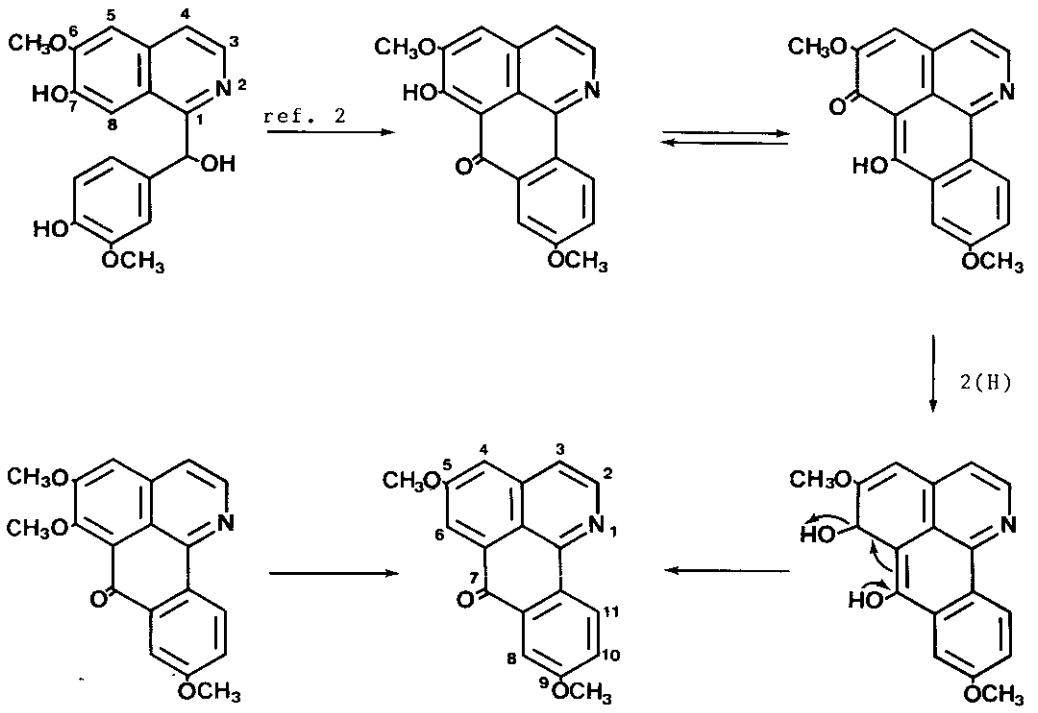
Jun-ichi Kunitomo* and Yohko Miyata
Faculty of Pharmaceutical Sciences, Mukogawa Women's University,
4-16, Edagawa-cho, Nishinomiya 663, Japan

Abstract ——— The structure of bianfugecine was unequivocally represented by formula (2) by chemical correlation of bianfugecine (2) with structurally established menisporphine (1).

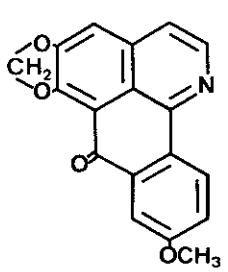
At the present time, five oxoisoaporphine type alkaloids possessing a new 7H-dibenzo[de, h]quinolin-7-one skeleton have been isolated from Menispermum dauricum DC. (Menispermaceae).[2-5] Their structural establishment depended mainly on comparison of their proton nuclear magnetic resonance (^{1}H-NMR) spectra with those of the corresponding oxoaporphine type alkaloids.[2,4] For example, menisporphine (1) and bianfugedine (3) were compared with 1,2,9-trimethoxyoxoaporphine (4) and lanuginosine (5), respectively. Unequivocal evidence, however, for the structure of this type alkaloids came from their synthesis[2,5] and chemical correlation of the alkaloid concerned with structurally established this type alkaloid.[5]

The studies on the alkaloidal constituents of the same plant in China resulted in isolation of bianfugecine (2). The oxoaporphine type alkaloid possessing the same functional groups as those of bianfugecine having the oxoisoaporphine skeleton has not been known and the structure of bianfugecine was presumed only by comparison of ^{1}H-NMR data of bianfugecine with those of menisporphine (1) and lanuginosine (5).[4] Therefore, more unequivocal structural proof was required. In the present paper, the authors wish to report chemical correlation of bianfugecine (2) with menisporphine (1), which provided further evidence for the structure of bianfugecine (2).

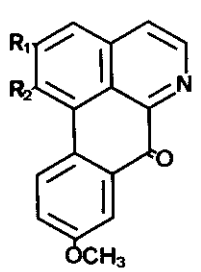
Catalytic hydrogenation of menisporphine (1) in the presence of platinum oxide as catalyst in acetic acid afforded yellow plates, mp 199-201°C. Compared with the ^{1}H-NMR spectrum of this product with that of menisporphine (1), the most low-



(1) (2)

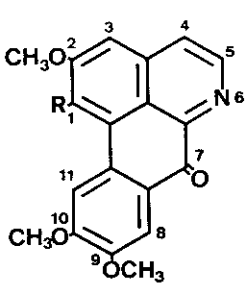


(3)



(4) $R_1 = R_2 = OCH_3$

(5) $R_1 + R_2 = OCH_2O$



(6) $R = OCH_3$

(7) R = H

field methoxyl signal of menisporphine (1) at δ 4.15 disappered in the spectrum of the product and in the aromatic proton region, a singlet (δ 7.40) due to C_4-H in menisporphine (1) appeared as a doublet (J = 2.5Hz) at δ 7.37 in the product, and one additional aromatic proton signal appeared at δ 8.22 as a doublet (J = 2.5Hz) in the product. Accordingly, this product is represented by 5,9-dimethoxy-7H-dibenzo[de, h]quinolin-7-one (2), which was generated by removal of the most hindered methoxyl group at the C-6 of menisporphine (1), and the analogous demethoxylation by catalytic hydrogenation had occurred in the case of 1,2,9,10-tetramethoxyoxoaporphine (6) to afford 2,9,10-trimethoxyoxoaporphine (7).[6] All spectral data of this product [ultraviolet (UV) spectrum, infrared (IR) spectrum, ^{1}H-NMR and mass spectra (MS)] were superimposable with those of the naturally occurring bianfugecine. Consequently, the structure of bianfugecine is now unequivocally represented by the formula (2). The biogenetic route for bianfugecine (2) in plant is probably shown in chart. In this biogenetic pathway, removal of the O-substituent at the C-7 position of the benzyltetrahydroisoquinoline is very seldom except the morphine-thebaine type alkaloids.

EXPERIMENTAL

The melting point was measured on a micro melting point hot stage apparatus and are uncorrected. UV and IR spectra were recorded on a Hitachi 323 spectrophotometer (in the solution of 95% EtOH) and on a JASCO IR-G spectrometer (in $CHCl_3$), respectively. ^{1}H-NMR spectra were recorded on a JEM-FX 200 spectrometer in $CDCl_3$, with tetramethylsilane as an internal standard. Abbreviations used: s = singlet, d = doublet. MS were determined using a Hitachi RMU-6E instrument with a direct inlet system. Column and preparative TL chromatographies were performed by the use of Merck Silica gel 60 (70-230 mesh) and 0.25 mm thick Merck Silica gel 60F-254, respectively.

Catalytic Hydrogenation of Menisporphine (1) A mixture of menisporphine (1) (16.1 mg) and platinum oxide (ca. 5 mg) in acetic acid (5.0 ml) was stirred at room temperature under a hydrogen atmosphere for 1 h. The catalyst was removed by filtration and the filtrate was made alkaline with 10% aqueous NH_4OH solution and extracted five times with CH_2Cl_2. The extract was washed with water, dried over $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography; elution of the column with ethyl acetate-$CHCl_3$ mixture (1:5) gave crystals,

which were recrystallized from MeOH to afford as yellow plates, mp 199-201°C [Yield 11.0 mg (75.4%)]. UV λ_{max}^{EtOH} nm (log ε): 254 (4.54), 268 (sh, 4.34), 288 (4.26), 291 (sh, 4.25), 318 (4.25), 331 (sh, 4.27), 382 (sh, 4.32), 420 (4.37). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1655 (-C=C-C=O), 1610. ^{1}H-NMR ($CDCl_3$) δ: 3.96 (3H, s, OCH_3), 4.01 (3H, s, OCH_3), 7.31 (1H, dd, J = 3.0, 9.0Hz, C_{10}-H), 7.37 (1H, d, J = 2.5Hz, C_4-H), 7.55 (1H, d, J = 5.5Hz, C_3-H), 7.81 (1H, d, J = 3.0Hz, C_8-H), 8.23 (1H, d, J = 2.5Hz, C_6-H), 8.61 (1H, d, J = 5.5Hz, C_2-H), 8.79 (1H, d, J = 9.0Hz, C_{11}-H). MS m/z (%): 291 (M^+, base peak), 290 (M^+-1, 10.0), 276 (M^+-CH_3, 16.8), 261 (M^+-CH_2O, 9.7), 248 (276-CH_3-CO, 6.4), 233 (2.6), 220 (11.1), 190 (6.2), 177 (9.3), 146 (1.1). Anal. Calcd for $C_{18}H_{13}NO_3$: C, 74.21; H, 4.50; N, 4.81. Found: C, 74.74; H, 4.43; N, 4.80.

ACKNOWLEDGEMENT

The authors wish to express their thanks to Miss K. Suwa, of our university, for elemental analyses and measurements of ^{1}H-NMR and MS.

REFERENCES AND NOTE

1) This paper constitutes Part 286 in the series "Studies on the Alkaloids of Menispermaceous Plants" and Alkaloids of Menispermum dauricum DC. (11). [Part 285: J. Kunitomo, Y. Miyata, and M. Oshikata, Chem. Pharm. Bull., in press. (10): See reference 5)].

2) J. Kunitomo, M. Satoh, and T. Shingu, Tetrahedron, 39, 3261 (1983).

3) M. Takani, Y. Takasu, and K. Takahashi, Chem. Pharm. Bull., 31, 3091 (1983).

4) C-Y. Hou and H. Xue, Acta Pharm. Sinica, 20, 112 (1985).

5) J. Kunitomo, S. Kaede, and M. Satoh, Chem. Pharm. Bull., 33, 2778 (1985).

6) J. Cohen and W. I. Taylor, J. Org. Chem., 28, 3567 (1963).

Received, 7th November, 1985