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A NEW APORPHINE ALKALOID, FISSOLDINE FROM FISSISTIGMA OLDHAMII (HEMSL.) MERR.

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Abstract-A new aporphine alkaloid, fissoldine, has been isolated from Fissistigma oldhamii and elucidated as (R)-1,2-methylenedioxy-9-methoxy-11-hydroxynoraporphine (3) by the spectral and chemical evidences.

Fissistigma oldhamii (Hemsl.) Merr. (Annonaceae) is a perennial climbing shrub which distributes mainly in southern China and Taiwan[1]. Until now there is not any report about the alkaloids of Fissistigma genus plants. Therefore, it is our object to clarify the alkaloid components of the plants growing on the latifoliate tree zone in Taiwan. Up to now, we have isolated one new aporphine alkaloid[2,3], fissoldine, in addition to two known aporphine alkaloids, xylopine (1) (main base) and N-norxylopine (2) from the plants. This paper will report the structural elucidation of fissoldine (3).

The hydrobromic acid salt of fissoldine (3) which is an amorphous powder was light grayish needles with mp 276-277°C (EtOH), $C_{18}H_{17}NO_4.HBr$, $[\alpha]_D^{25}$ -99.1° (c=0.45, EtOH), $\lambda_{max.}^{EtOH}$ 216, 273 and 295 nm (log ε 4.55, 4.03 and 4.15), and $\nu_{max.}^{KBr}$ 3275 (OH), 1042 and 945 cm^{-1} (OCH_2O) exhibits a methylenedioxylated aporphine system. The uv spectral curve of fissoldine showed bathochromic shift by adding KOH solution, and the Gibbs test for fissoldine showed positive. Moreover, in the mass spectrum there are intensive fragments at m/z 294, 282, 252, 238, and 224 in addition to 311 (M^+) and 310 (base peak). The fragment of m/z 282 (ion 7) was obtained by the retro-Diels-Alder fragmentation[4] of aporphinoid alkaloids. In the 'Hnmr spectrum ($CDCl_3$), there are the chemical shifts of the methoxyl group at δ 3.80 (3H, s), methylenedioxyl group at δ 5.96 and 6.06 (each 1H, s), and three aromatic protons of C-3,8 and 10 position at δ 6.43 (1H, s), 6.47 (1H, s) and 6.57 (1H, s), respectively, and there are no signals corresponding to N-methyl group and to C-11 proton at lower field. The above data suggested that the four oxygens of fissoldine are located at the 1,2,9 and 11 positions in the aporphine skeleton.

When fissoldine was treated with formalin and sodium borohydride, an almost colorless oily base, N-methylfissoldine (4) which has a signal corresponding to N-methyl group at δ 2.50 in the 'Hnmr ($CDCl_3$) was obtained. The hydrobromide of 4 is light brownish needles with mp 236-239 C° (MeOH),

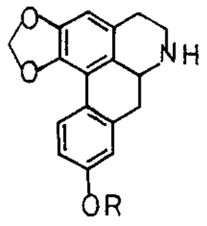
$C_{19}H_{19}NO_4$.HBr, and m/z 325 (M^+), 324 (base peak), and 282 (ion 7). The O-methylation of 4 with diazomethane gave light yellowish brown oily base, N,O-dimethylfissoldine (5) with $[\alpha]_D^{29}$ -207° (c=0.5, $CHCl_3$), and two methoxyl groups at δ 3.82 and 3.86 (each 3H, s) in the 'Hnmr ($CDCl_3$). From the above results, it was presumed that the phenolic hydroxyl group of fissoldine attached on the C-11 position. In order to make the positions of the four oxygens clear, the dehydroxylation method appeared on the literatures5,6) was carried out for fissoldine (3).

When the almost colorless amorphous fissoldine 1-phenyltetrazole ether (6) obtained by the reaction of 3 and 1-phenyl-5-chlorotetrazole were treated with palladium-charcoal-H_2 an almost colorless amorphous base with $[\alpha]_D^{25}$ -50° (c=0.5, EtOH) was obtained as the dehydroxylation product which is insoluble in dilute NaOH solution.

In the 'Hnmr spectrum ($CDCl_3$) of the dehydroxylation product, the signals corresponding to C-11 aromatic proton appeared as a doublet at δ 7.94 (1H, d, j=10.0 Hz). Moreover, the signal at δ 6.57 corresponding to C-10 proton of 3 was disrupted to a doublet [δ 6.72 (1H, d, j=10.0 Hz)] by coupling with C-11 proton. This 'Hnmr spectrum was similar to that of xylopine (1)7).

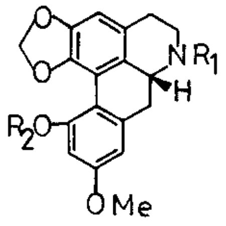
Therefore, the dehydroxylation product was compared with the authentic sample of xylopine (1). The result was that the uv (EtOH), ir ($CHCl_3$), and tlc were all identical.

By these facts, the chemical structure, 1,2-methylenedioxy-9-methoxy-11-hydroxynoraporphine (3) was offered for fissoldine, and the absolute configuration at 6a is R-configuration because of the (-)-rotation.



1 R=Me

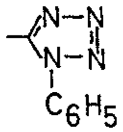
2 R=H

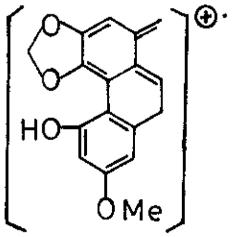


3 R1=R2=H

4 R1=Me , R2=H

5 R1=R2=Me

6 R1=H , R2= 



7 m/z 282

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