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ALKALOIDS OF LIMACIA CUSPIDATA

THE STRUCTURES OF THREE NEW BISBENZYLISOQUINOLINE ALKALOIDS.

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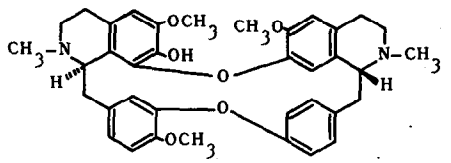
Three new phenolic bisbenzylisoquinoline alkaloids for which we proposed the name limacine, limacusine, and cuspidaline, were isolated from Limacia cuspidata (Miers) Hook. f. et Thom. (Menispermaceae) collected in Borneo. We now wish to report the characterisation of these alkaloids (I, II, and IV).

Limacine (I) crystallized from acetone as colorless needles, m.p. 154-156°, $[\alpha]_D$-212°($CHCl_3$), $C_{37}H_{40}O_6N_2$. The NMR spectrum* showed two N-methyl groups (7.67, 7.40τ) and three methoxyl groups (6.67, 6.25, 6.08τ). Its NMR and IR** spectra were found to be superimposable with those of fangchinoline (antipodal structure of I)[1]. Other properties of limacine and fangchinoline were also identical except the sign of the specific rotations.



I

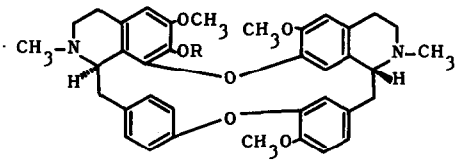
* All NMR spectra were run in $CDCl_3$ on a Varian A-60 spectrometer with TMS as internal standard.

** All IR spectra were measured in $CHCl_3$ solution.

Accordingly, limacine must be assigned the structure I , which is enantiomeric with fangchinoline.

Limacusine (II) crystallized from methanol as colorless prisms, m.p. 235-237°, $[\alpha]_D$+110°($CHCl_3$), $C_{37}H_{40}O_6N_2$. The NMR spectrum revealed the presence of two N-methyl groups (7.48, 7.53τ) and three methoxyl groups (6.67, 6.25, 6.05τ). Methylation of limacusine with diazomethane afforded O-methyllimacusine as colorless needles, m.p. 210-212°, $[\alpha]_D$+90°($CHCl_3$), which was identical (IR and mixed m.p.) with the authentic sample of N-methyldihydroepistephanine-B (O-methylrepandine antipode)(III)[2].

Bick et al.[3] showed that in the NMR spectra(in $CHCl_3$) of bisbenzylisoquinoline alkaloids, methoxyl groups at 7-position of the isoquinoline moiety have consistently higher chemical shifts (6.80-6.98τ) than those at other positions. In the NMR spectrum of limacusine, all methoxyl signals appears between 6.67τ to 6.05τ. Absence of the higher field signal due to the methoxyl at 7-position indicates that the hydroxyl group of limacusine is located at 7-position in the isoquinoline moiety of N-methyldihydroepistephanine-B (III). The structure of limacusine must, therefore, be represented by formula II.



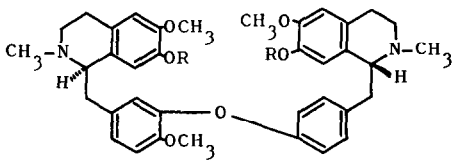
II : R = H
III : R = CH_3

Further evidence for the structural assignment II to limacusine was provided by the mass spectrometry*. The base

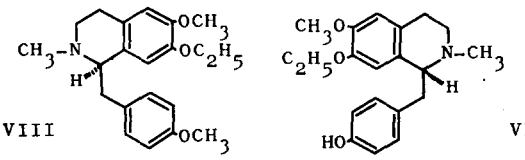
* Mass spectrum was taken with Hitachi Mass Spectrometer RMU. 6D equipped with direct inlet system (MG-150).

peak in the spectrum is a doubly charged fragment at m/e 191 derived from the two isoquinoline rings of the alkaloid. Additional peaks occur at m/e 382, 381, 367, 175, 174, 168, and 141. This fragmentation pattern is a strong support for the structure II .[4)]

Cuspidaline (IV) was obtained as a colorless oil or as an amorphous styphnate. The free base showed $[\alpha]_D$-48°($CHCl_3$). The NMR spectrum of the free base revealed the presence of two N-methyl groups (7.56, 7.52τ) and three methoxyl groups (6.19τ). O-Methylation of cuspidaline with diazomethane gave an amorphous O,O-dimethyl ether (methiodide, m.p. 181-184°). In the NMR spectrum, O,O-dimethylcuspidaline gave rise to two additional methoxyl signals at 6.42τ and 6.38τ, together with two N-methyl (7.52, 7.47τ) and three methoxyl (6.22, 6.20, 6.18τ) signals. It was found to be identical with the known alkaloid O-methyldauricine (V)[5)] by the direct comparisons of their IR and NMR spectra.



IV : R = H
V : R = CH_3
VI : R = C_2H_5



VIII VII

Treatment of cuspidaline with diazoethane led to O,O-diethylcuspidaline (VI). Metallic sodium in liquid ammonia cleavage of VI was found to yield two coclaurine type bases.

The one was found to be phenolic base, which was given as colorless needles, m.p. 129-131°, $[\alpha]_D$-90°($CHCl_3$). This substance was identified as D-1-(4-hydroxybenzyl)-2-methyl-6-methoxy-7-ethoxy-1,2,3,4-tetrahydroisoquinoline (VII)[6] by IR and NMR comparisons. The other, non-phenolic base, was obtained as a crystalline oxalate, m.p. 171-173°, $[\alpha]_D$-110°(MeOH). It was proved to be identical with D-1-(4-methoxybenzyl)-2-methyl-6-methoxy-7-ethoxy-1,2,3,4-tetrahydroisoquinoline (VIII) prepared from VII and diazomethane, by IR and NMR comparisons of their free base.

On the basis of these experimental evidences, the structure of cuspidaline should be assigned to the formula IV .

The biogenetical relationship between these three alkaloids would be understood by the assumption that intramolecular dehydrogenative coupling[7] of cuspidaline (IV) gave rise both to limacine (I) and to limacusine (II).

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