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CEPHARAMINE:

A NEW HASUBANAN ALKALOID FROM STEPHANIA CEPHARANTHA

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From Stephania cepharantha Hayata, a new phenolic alkaloid, cepharamine, has been isolated.

Cepharamine, $C_{19}H_{23}O_4N$, M.W. 329 (mass spectrum: M^+329), m.p. 186-187°(uncorr.), $[\alpha]_D$-248°(chloroform), UV:λ_{max} 259 mμ (logϵ: 3.82)*1, IR*1: 1685 cm^{-1}(-CO-$\overset{|}{C}$=CH-), 1630 cm^{-1}(enolic double bond) and 3470 cm^{-1}(OH), NMR*2: 7.59 (3H, s.,-$\overset{|}{N}$-$\underline{CH}_3$), 6.15 (3H, s.,-O-$\underline{CH}_3$), 6.35 (3H, s.,-O-$\underline{CH}_3$), 6.27 (1H, d., J=16 cps); 7.50 (1H, d., J=16 cps)-$\overset{|}{\underset{|}{C}}$-$\underline{CH}_2$-CO-, 4.38 (1H, s., -$\overset{|}{C}$=$\underline{CH}$-), 4.00 (1H, s.,-$\underline{OH}$), 3.33 (1H, d., J=8 cps); 3.40 (1H, d., J=8 cps) two aromatic protons. Cepharamine shows strong blue colouration on Gibbs' reagent.

Reduction of cepharamine with sodium borohydride yielded a mixture of two epimeric dihydrocepharamines (II).

Treatment of (II) with dil. hydrobromic acid gave the hydroxyketone (III) in good yield, IR: 1710 cm^{-1}(six membered saturated ketone; no absorption for enolic double bond).

(III) was acetylated by Ac_2O-pyridine to give the diacetyl derivatives, IR: 1770 cm^{-1}, 1725 cm^{-1}(OAc), which were reduced by Huang-Minlon procedure followed with catalytic hydrogenation over PtO_2 to afford a saturated compound (IVa). This compound (IVa) revealed the presence of a N-methyl group (7.81, 3H) and a methoxyl group (6.18, 3H) in the NMR spectrum and showed strong blue colouration on Gibbs' reagent.

Direct proof of the structure (IVa) was achieved by comparison of (IVa) with an authentic sample of the compound (IVb)[1]. The IR, NMR and TLC[*3] of (IVa) were found to be identical with those of (IVb); the ORD measurement showed that (IVa) is antipodal with (IVb).

Therefore, the evidence that cepharamine has the hasubanan skeleton with C_3-methoxyl and C_4-hydroxyl groups was furnished.

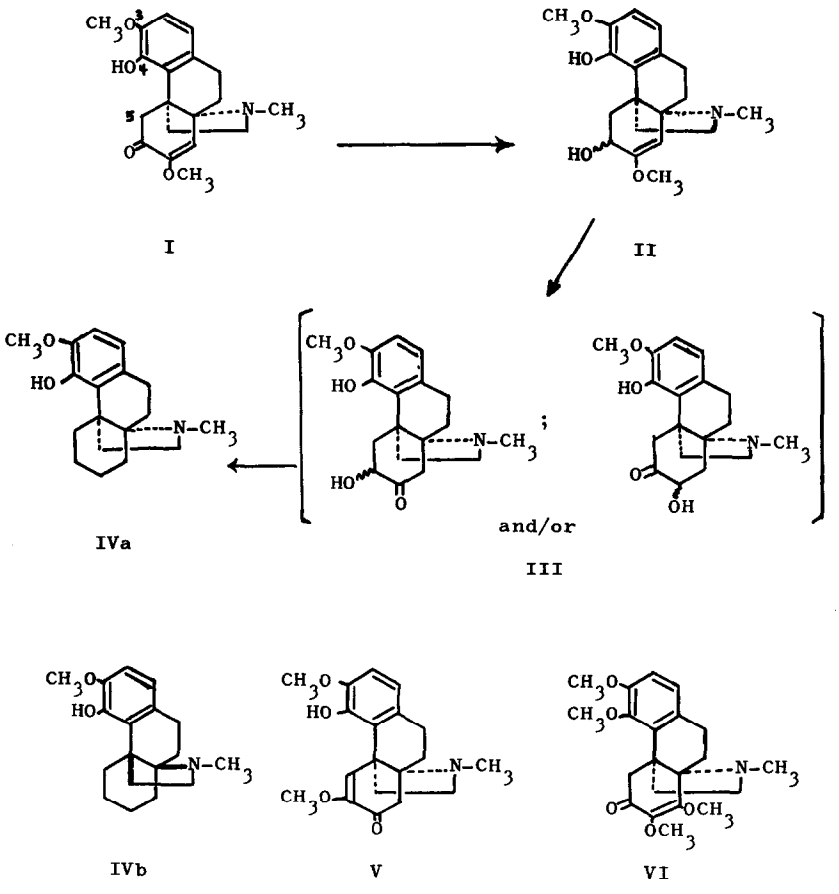
The formulae other than (I) and (V) are excluded for cepharamine from the NMR data combined with the fact that no conjugated ketone was obtained on the dil. hydrobromic acid treatment of dihydrocepharamines (II).

Hasubanonine (VI), which has an active methylene group on C_5 of its hasubanan skeleton, shows one of the active hydrogens at 6.62τ and another at 7.27τ in its NMR spectrum[1]

The NMR spectrum of cepharamine also showed the peaks at 6.27 and 7.50τ, due to an active methylene. The similarity of the lower field appearance of one proton of the active

methylene in the NMR spectra of (I) and (VI) makes the assignment reasonable that the active methylene of cepharamine exists at C_5 of its hasubanan skeleton.

On the basis of these results, we propose the structure (I) for cepharamine.



FOOTNOTES

*1 Unless otherwise noted, IR spectra were measured in chloroform solution and UV spectra were obtained in ethanol solution.

*2 All NMR spectra were taken on a Varian Associates recording Spectrometer (A-60) at 60 Mc. in $CDCl_3$. Chemical shifts are reported in τ values, using tetramethylsilane as an internal standard. Abbreviations used for the multiplicity of the signals: s.=singlet, d.=doublet.

*3 Thin Layer Chromatography: a) Silica gel G according to Stahl, solvent, chloroform:methanol (1:1). b) Aluminium oxide G according to Stahl, solvent, chloroform c) Aluminium oxide G according to Stahl, solvent, chloroform:acetone (1:1).

REFERENCE

1) M. Tomita, T. Ibuka, Y. Inubushi, Y. Watanabe, M. Matsui, Tetrahedron Letters No. 40, 2937 (1964); idem. Chem. Pharm. Bull. (Tokyo) 13, 538 (1965).