BISAKNADININE, A NEW DIMERIC HASUBANAN ALKALOID FROM *Stephania Sasakii* Hayata

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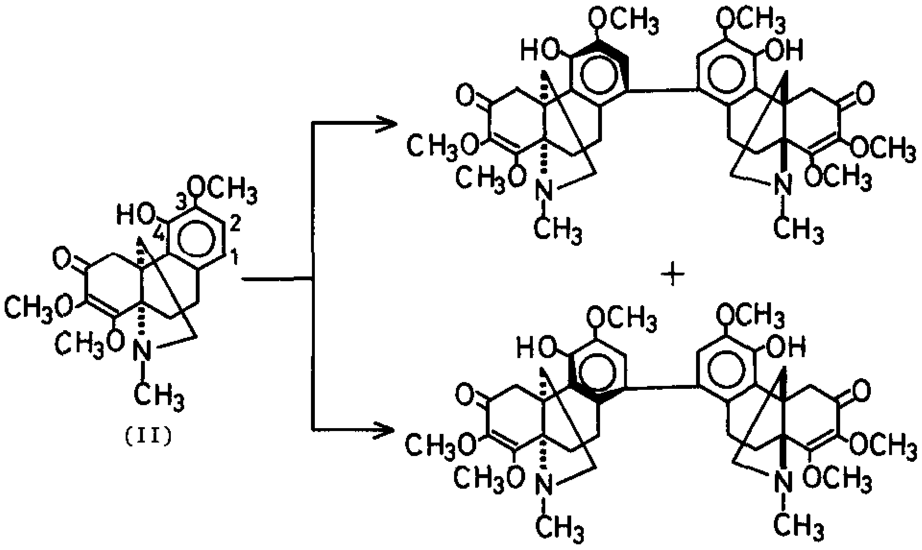
A new type base, bisaknadinine, was isolated from *Stephania Sasakii* Hayata, and its structure was decided as (I) from spectral data, especially by the application of nuclear Overhauser effect and internuclear double resonance. The chemical oxidation of aknadinine (II) afforded bisaknadinine (I), thus the absolute configuration of (I), except the steric configuration concerning the mode of biphenyl linkage, was proved.

In the previous papers$^{1,2)}$, the isolation of several bases from *Stephania Sasakii* Hayata (Menispermaceae) was reported. Recently, a new type base, bisaknadinine was newly isolated. This communication describes the structure elucidation of this base.

Bisaknadinine (I) was recrystallized from acetone as colorless needles, showing a single spot on TLC, mp 198∿200°, $[\alpha]_D$:-253.3°($CHCl_3$), UV spectrum: λ_{max}^{EtOH} 263nm (log ε, 4.32), 293(sh., 4.00), λ_{min}^{EtOH} 243(4.22). Its IR spectrum(KBr) shows conjugated ketone and hydroxyl group at 1660 and 3350cm^{-1}, respectively. Its NMR spectrum($CDCl_3$) reveals signals for N-methyl group (δ 2.48), methoxyl groups (δ 3.66, 3.83, 4.06), hydroxyl group (δ 6.06) and aromatic proton (δ 6.57). The NMR data are closely similar to those of aknadinine (4-demethylhasubanonine)(II)$^{3)}$ except the relative intensity of aromatic proton being reduced to one half. The mass spectrum shows the molecular ion peak at m/e 716.8. Those facts suggested



(II)

(I)

that the dimer was composed of two identical radicals lacking one aromatic proton from aknadinine (II).

In order to determine the bonding position of aromatic rings of (I), nuclear Overhauser effect (NOE) and internuclear double resonance (INDOR) were applied. In the INDOR experiment of bisaknadinine (I), the peak was observed at δ 3.83 (methoxyl group) by monitoring the signal of the aromatic proton at δ 6.57. This observation indicates the presence of NOE effects (16.8% increment) due to *ortho* position relationship between an aromatic proton and a methoxyl group. This compound was negative with 2,6-dichloroquinone-4-chlorimide (Gibb's reagent) in opposition to aknadinine (II). On the basis of these findings, it is concluded that the position of biphenyl bond is C-1 of (II).

Finally, evidence for the structure including absolute configuration of bisaknadinine (I) was given by the correlation with aknadinine (II) as following. Treatment of aknadinine (II) with silver nitrate solution, as to disinomenine from sinomenine4) gave dimeric compound, which was identified with natural bisaknadinine (I) by direct comparison of IR spectrum (KBr), TLC, specific rotation and mixed melting point. From the reaction products, its stereoisomer (colorless oil, $[\alpha]_D$: -125.0°($CHCl_3$)) was also obtained in low yield.

Recently, Brossi et al.5) have measured the CD and ORD spectra of disinomenine and ψ-disinomenine and discussed the absolute configuration concerning the mode of biphenyl linkage. The ORD ($[\phi]_{295}$:-81203°(tr.), $[\phi]_{244}$:+124193°(pk.)) and the CD ($[\theta]_{315}$:+45378°(pk.), $[\theta]_{265}$:-102698°(tr.), $[\theta]_{234}$:+119417°(pk.)) data of bisaknadinine (I) are closely similar to those of so called ψ-disinomenine, but the absolute configuration concerning the mode of biphenyl linkage of (I) is not decided at present.

Bisaknadinine (I) must be produced by *para* oxidative coupling of the phenolic group of aknadinine (II) and constitutes first example of dimeric hasubanan type alkaloid.

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