ALKALOIDS OF *STEPHANIA HERNANDIFOLIA*. III

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From the roots of the tropical plant *Stephania hernandifolia* [*St. intertexta* Miers, *Cisampelos hernandifolia* Willd, *C. discolor* D.C., *Clypea hernandifolia* W. Prodr. (family Menispermaceae)] have been isolated the alkaloids fangchinoline, isochondodendrine (isobeerine), dl-tetrandrine, l-tetrandine [1], isotrilobine, and an alkaloid of the composition $C_{35}H_{34}O_6N$ [2]. We have studied the composition of the alkaloids of the herb *Stephania hernandifolia* Walp. from the Black Sea coastal region of the Caucasus (grown at the Zonal Experimental Station of the All-Union Scientific Research Institute for Medicinal Plants) collected in October 1965. The total alkaloids (0.6%) isolated by the dichloroethane method were shown by thin-layer chromatography [alumina; ether-methanol (25 : 1) system] contain seven substances with R_f 0.95, 0.86, 0.73, 0.63, 0.56, 0.50, and 0.41.

Alkaloid (I) present in the plant in large amount was obtained by chromatography on alumina. The noncrystalline base with the composition $C_{20}H_{25}O_5N$ formed a crystalline perchlorate corresponding to the formula $C_{20}H_{25}O_5N \cdot HClO_4$. The alkaloid contains a $-NCH_3$ group. The five oxygen atoms in the molecule of this alkaloid are distributed among a conjugated carbonyl group, three methoxy groups, and a hydroxy group. The presence of the latter is confirmed by the preparation of an O-acetyl derivative $C_{22}H_{27}O_6N$ (II). The position of the absorption band of the acetyl carbonyl group in the IR spectrum of the substance (1775 cm^{-1}), the solubility of the alkaloid in alcohols, and the positive reaction with ferric chloride show the phenolic or enolic nature of the hydroxyl.

When the base was heated with methyl iodide, a methyl ether $C_{21}H_{27}O_5N$ (III) was formed, giving an IR spectrum lacking the band at 3400 cm^{-1}. The action of methyl iodide on the base (III) gave the methiodide of the O-methyl derivative $C_{21}H_{27}O_5N \cdot CH_3I$ (IV).

The properties of the alkaloid (I) that have been considered indicate that it is a new substance, and we have called it hernandoline. The composition of this base and its derivatives show the possibility of assigning it to the group of alkaloids related to sinomenine or hasubanonine found in plants of the family Menispermaceae [3,4].

To confirm this assumption we used the cleavage method known for alkaloids of the type of homostephanoline, hasubanonine, and prometaphenine [4–7] leading to the isolation of phenanthrene derivatives and consisting of the acetolysis of the des base formed by Hofmann degradation.

The acetolysis of the des base obtained from substance (IV) gave a substance $C_{20}H_{18}O_6$ (V) containing two $-OCH_3$ and two $-OCOCH_3$ groups. The empirical formula of the product (V), $C_{14}H_6(OCH_3)_2(OCOCH_3)_2$, corresponds to the formula for a diacetoxydimethoxyphenanthrene. The UV spectrum of this substance λ_{max} 228, 259, 283, 301, 313, 342, 360 (log ε 4.35; 4.67; 4.22; 4.08; 4.10; 3.24; 3.18, respectively) is similar to that of 1,2-diacetoxy-5,6-dimethoxyphenanthrene [8], which indicates the identity of the main skeleton of these derivatives. Hernandoline probably has a morphinan nucleus or else it belongs to the alkaloids of the hasubanonine type.

Experimental

The IR spectra of the substances were taken on a UR-10 spectrophotometer in paraffin oil. The UV spectra were obtained on a SF-4 spectrophotometer (in alcohol). All the melting points are uncorrected.

Hernandoline (I). 15 kg of the dried comminuted herb *St. hernandifolia* were steeped in 10% ammonia and exhaustively extracted with dichloroethane. The bases were extracted from the dichloroethane solution with 10% sulfuric acid. The sulfuric acid extract was neutralized with ammonia to pH 6.5–7, and the alkaloids were extracted with ether. After being dried with sodium sulfate, the ethereal extract was evaporated to the state of a viscous sirup and passed through a column of alumina (activity grade II). When the column was washed with ether, the first portions of eluate yielded 15 g of hernandoline. Yield 0.1% of the air-dry herb. Thin-layer chromatography of the substance [alumina; ether–methanol (25 : 1)] gave a single spot with R_f 0.86.

Hernandoline perchlorate. A saturated solution of sodium perchlorate was added to a solution of 0.3 g of hernandoline in 3% hydrochloric acid. This gave the perchlorate of the alkaloid with mp 225°–226° C (alcohol).

Found, %: C 52.07, 52.02; H 5.76, 5.76; N 2.93, 2.91; Cl 8.49, 8.20; OCH_3 20.36, 2055; NCH_3 3.21, 3.85. Calculated for $C_{20}H_{25}O_5N \cdot HClO_4$, %: C 52.23; H 5.66; N 3.04; Cl 7.72; 3 OCH_3 20.22; NCH_3 3.26.

From the perchlorate a noncrystalline base with $[\alpha]^{21}_D$ $-44°$ (c 0.95; ethanol) was isolated. IR spectrum: 3400, 1670, 1610 cm^{-1}.

O-Acetylhernandoline (II). A solution of 0.2 g of the base in 1.5 ml of pyridine was treated with 1 ml of acetic anhydride. The mixture was left at 20° C for 14 hr. After recrystallization from a mixture of hexane and ether, the reaction product had mp 113.5°–114° C. IR spectrum: 1775 (O-acetyl), 1670 cm^{-1}.

Found, %: C 65.97, 66.14; H 6.88, 6.91; N 3.59, 3.66; equiv. wt. 399.2 (potentiometric); mol. wt. 460 (Rast). Calculated for $C_{22}H_{27}O_6N$, %: C 65.83; H 6.73; N 3.49; mol. wt. 401.

Methyl ether of hernandoline (III). A solution of 0.3 g of (I) in 5 ml of acetone was treated with 1 ml of methyl iodide, and the mixture was heated in a water bath at 65°–75° C for 3 hr. O-Methylhernandoline hydriodide with mp 186° C (acetone) was formed. For conversion into the base, the solution of the hydriodide was brought to pH 9–10 and the O-methylhernandoline (III) was extracted with ether, mp 104° C (ether).

Found, %: C 67.94, 68.16; H 7.43, 7.39; N 3.69, 3.75. Calculated for $C_{21}H_{27}O_5N$, %: C 67.56; H 7.24; N 3.53.

O-Methylhernandoline methiodide (IV). A solution of 0.45 g of (III) in acetone was treated with 1.5 ml of methyl iodide and the mixture was heated in a water bath at 65°–75° C for 4 hr. After recrystallization from a mixture of alcohol and acetone, the methiodide had mp 190°–191° C. The substance was dissolved in water but the reaction product did not pass into ether from the aqueous solution at pH 9–10, which distinguished it from (III).

Found, %: C 50.88; H 5.93; N 2.46, 2.45; I 24.91. Calculated for $C_{21}H_{27}O_5N \cdot CH_3I$, %: C 50.30; H 5.71; N 2.66; I 24.2.

Hofmann degradation of (IV) and acetolysis of the des-O, N-dimethyl-hernandoline. Freshly prepared silver oxide (from 0.8 g of $AgNO_3$) was added to a solution of 1.2 g of (IV) in water, and the mixture was shaken for 5 hr. The silver iodide that had precipitated was filtered and the solvent was distilled off. The residue was crystallized from alcohol, mp 270°–271° C. The des-O, N-dimethylhernandoline hydrochloride melted at 244° C (alcohol). A mixture of 0.6 g of the des base, 8 ml of acetic anhydride, and 0.8 g of anhydrous sodium acetate was boiled for 1.5 hr. After the mixture had cooled, the sodium acetate was filtered, 20 ml of methanol added to the filtrate, and the solvent evaporated. The dry residue was dissolved in 5% sulfuric acid and the reaction product was extracted with ether. The extract was passed through a column of alumina (activity grade II). This gave 0.12 g of a nitrogen-free product with mp 163° C. IR spectrum: 1790 cm^{-1}. The presence of two acetoxy groups was found by the transesterification method and gas chromatography.

Found, %: C 67.83, 67.93; H 5.25, 5.33; OCH_3 17.5, 17.15. Calculated for $C_{20}H_{18}O_6$, %: C 67.80; H 5.05; 2 OCH_3 17.5.

The spectra were taken by M. E. Perel'son's group. The elemental composition was determined by E. A. Nikonova's group and the acetoxy groups by V. S. Kabanov.

Summary

1. A new alkaloid hernandoline with the composition $C_{20}H_{25}O_5N$ has been isolated from the herb *Stephania hernandifolia* Walp.

2. The Hofmann degradation of the methiodide of the O-methyl ether of hernandoline has given a des base acetolysis of which led to the formation of a dimethoxydiacetoxyphenanthrene.

3. It has been suggested that hernandoline is similar to alkaloids related to sinomenine and hasubanonine.

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