d-CAAVERINE AND A NEW ALKALOID – LIRINIDINE – FROM Liriodendron tulipifera

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Continuing the separation of the phenolic fraction of the mixed bases of the leaves of L. tulipifera L. [1] on a column of silica gel, we have isolated a base (I) and a new alkaloid which we have called lirinidine (II).

Base (I) was a crystalline substance with the composition $C_{17}H_{17}NO_2$, mp 207-209°C (decomp.), $[\alpha]_D^{22}$ +95° (c 0.12; methanol). Its UV spectrum [λ_{max} 273, 313 nm (log ε 4.19, 3.70)] is characteristic for disubstituted aporphine alkaloids [2]. The IR spectrum showed absorption bands at (cm^{-1}) 3310 (OH and NH groups), 1610, 1505 (aromatic ring), 2845, 1250 (methoxy group), and 1385, 1130.

The mass spectrum of the alkaloid had intense peaks of ions with m/e 267 M^+, 266 $(M-1)^+$ (100%), 252 $(M-15)^+$, 250 $(M-17)^+$, 238 $(M-29)^+$, 236 $(M-31)^+$, 223 $(M-44)^+$, which are characteristic of noraporphine bases [3].

In the NMR spectrum of (I) there is a signal in the form of a three-proton singlet at 6.17 ppm belonging to methoxy protons. In the weak-field region there is a one-proton singlet at 3.48 ppm (C_7 aromatic proton), a one-proton multiplet at 1.70 ppm (C_4 aromatic proton), and a three-proton multiplet at 2.70-2.95 ppm (aromatic protons).

The acetylation of the base (I) with acetic anhydride in pyridine gave a O,N-diacetyl derivative with mp 236-238°C (from acetone) with the composition $C_{21}H_{21}NO_4$, M^+ 351 (mass spectrometrically). The IR spectrum of this diacetyl derivative lacked an absorption band at 3310 cm^{-1} and had new absorption bands at 1625 cm^{-1} (N-acetyl group) and at 1760 cm^{-1} ($ArO-CO-CH_3$).

A comparison of the properties given above for (I) with literature information (Table 1) showed that the base (I) that we had isolated is the dextrorotatory form of caaverine [4].

Lirinidine (II) is an oily substance with the composition $C_{18}H_{19}O_2N$, $[\alpha]_D^{25}$ +78° (c 0.19; chloroform) giving a crystalline hydrochloride with mp 235-237°C (decomp.). Its UV spectrum [λ_{max} 230 (inflection), 271, 312 nm (log ε 4.22, 4.12, 3.67)] is similar to that of caaverine and of nuciferin [4, 5].

TABLE 1

Compound	Composition	mp, °C	$[\alpha]_D$, deg	Spectra
				UV spectrum, λ_{max}, nm
Caaverine	$C_{17}H_{17}O_2N$	208–210 (decomp.)	–85 (c 1; methanol)	272 (lg ε 4,25), 310 (lg ε 3,70).
The base (I)	$C_{17}H_{17}O_2N$	207–209 (decomp.)	+95 (c 0,12; methanol)	273 (lg ε 4,19). 313 (lg ε 3,70).
Caaverine O,N-diacetate	$C_{21}H_{21}O_4H$	236–238	—	IR spectrum, cm^{-1} 1625, 1760
O,N-Diacetate of the base (I)	$C_{21}H_{21}O_4N$	236–238	—	1625, 1760

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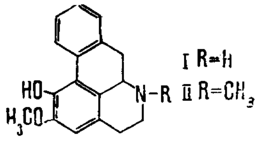
In the IR spectrum of the hydrochloride of (II) there are absorption bands at (cm^{-1}) 3200-3400 (hydroxy group), 2850, 1260 (methoxy group), 1610 (aromatic ring), and 781, 752.

In the mass spectrum of (II) there are strong peaks of ions with m/e 281 M^+, 280 $(M-1)^+$ (100%), and 238 $(M-43)^+$, which are characteristic of the aporphine alkaloids, and, in addition, the peaks of ions with m/e 266 $(M-15)^+$, 264 $(M-17)^+$, and 250 $(M-31)^+$, formed by the ejection of methyl, hydroxy, and methoxy groups from the molecular ion.

In the NMR spectrum of lirinidine there are the signals of an N-methyl group (a three-proton singlet at 7.53 ppm) and a methoxy group (three-proton singlet at 6.19 ppm) and, in the weak field, the signals of five aromatic protons. A one-proton singlet at 3.50 ppm relates to the C_7 proton and a one-proton multiplet at 1.73 ppm to the C_4 proton, while the signals of three aromatic protons appear in the spectrum in the form of a multiplet at 2.65-2.95 ppm. Hence, lirinidine has the following developed formula: $C_{16}H_{12}(>N-CH_3)$, $(-OH)$, $(-OCH_3)$.

On comparing the developed formulas of caaverine and lirinidine it can be seen that the latter differs from caaverine by one $N-CH_3$ group. In fact, when d-caaverine was methylated by Hess's method,a base identical with lirinidine was obtained. The facts given above enabled the structure 5-hydroxy-6-methoxyaporphine (II) to be established for lirinidine.



I R=H
II R=CH_3

EXPERIMENTAL

The mass spectra were taken on an MKh-1303 instrument with a glass inlet system at 40 eV, and the NMR spectra on a JNM-4H-100/100 MHz instrument with HMDS as internal standard (τ scale). The homogeneity of the substances was checked by chromatography in a thin layer of type KSK silica gel in the benzene–ethanol (4:1) system.

Separation of the Combined Alkaloids. The phenolic fraction (1.70 g) of the mixed bases was passed through a column of silica gel. On elution with benzene containing 1% of methanol, lirinine with R_f 0.62 and a mixture of bases (120 mg) with R_f 0.62 and 0.52 were obtained.

d-Caaverine (I). Subsequent elution with benzene containing 2% of methanol gave an alkaloid fraction (0.17 g) the recrystallization of which from acetone yielded substance (I) with mp 207-209°C (decomp.), R_f 0.23.

O,N-Diacetyl-d-caaverine. A mixture of 30 mg of caaverine, 0.5 ml of acetic anhydride, and two drops of pyridine was left at room temperature for three days. Then the acetic anhydride and the pyridine were evaporated off, the residue was dissolved in a small amount of water, and the solution was made alkaline and was extracted with ether. Distillation of the ether gave white acicular crystals with mp 236-238°C (from acetone), R_f 0.78.

Lirinidine (II). The mixture of bases (120 mg) was rechromatographed on a column, and the benzene–methanol (99:1) eluate yielded an oily base with R_f 0.52. Yield 75 mg.

Lirinidine Hydrochloride. When ethanolic solutions of lirinidine and hydrogen chloride were mixed in the presence of ether, the crystalline hydrochloride was obtained with mp 235-237°C (decomp.).

Methylation of d-Caaverine. A mixture of 30 mg of d-caaverine, 1.20 ml of 85% formic acid, and 2 ml of 36% formaldehyde was boiled for 4 h. After cooling, the reaction mixture was diluted with water and washed with ether. The aqueous layer was made alkaline and extracted with ether, and then the solvent was distilled off, giving a substance with R_f 0.52. From its R_f value and IR spectrum, this base proved to be identical with lirinidine.

SUMMARY

From the leaves of Liriodendron tulipifera have been isolated d-caaverine and a new aporphine alkaloid – lirinidine – with the composition $C_{18}H_{19}O_2N$, $[\alpha]_D^{25}$ +78° (c 0.19; chloroform).

On the basis of features of its UV, IR, NMR, and mass spectra and chemical transformations, the structure of 5-hydroxy-6-methoxyaporphine has been established for lirinidine.

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