ALKALOIDS OF LEONTICE ALBERTII

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From L. albertii Rgl. we have isolated thaspine [1], N-methylcytisine [2] and the new bases leontalbine, leontalbinine $C_{15}H_{22}N_2O$, albertine $C_{15}H_{22}N_2O_2$, and base (II) [3, 4]. Leontalbine has the structure *l*-5, 17-dehydromatrine [4].

The IR spectrum of leontalbine has absorption bands of a transquinolizidine (2800–2700 cm^{-1}), a double bond and the carbonyl of a lactone group (1665 w, 1640 cm^{-1}) in the form of the $-C{=}C-N{=}C-O$ chromophore; UV spectrum: λ_{max} 242 mμ [4–6].

The reduction of leontalbinine with lithium aluminum hydride and subsequent hydrogenation (Adams) of the deoxy base obtained gave deoxydihydroleontalbinine. A comparison of its mass spectrum and that of *l*-matridine showed that they are stereoisomers.

The catalytic hydrogenation of leontalbinine gives allomatrine. The formation of deoxydihydroleontalbinine and of allomatrine shows that leontalbinine isomerizes on hydrogenation in a similar way to matrine and sophoridine [7–9].

Leontalbinine perchlorate is not reduced by sodium borohydride, while deoxyleontalbinine perchlorate is reduced. Consequently, three possible positions remain for the double bond in the heterocyclic skeleton of matrine (C_5-C_{17}, C_7-C_{11}, and $C_{11}-C_{12}$).

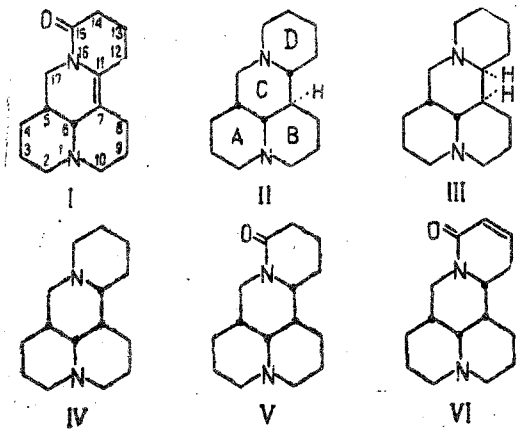
We have detected glutaric acid in the products of the oxidation of leontalbinine with chromic acid. Consequently, the double bond in the molecule of the alkaloid is present at C_7-C_{11}. This is also confirmed by the absence of the signal of an olefinic proton in the NMR spectrum of leontalbinine.

Both on reduction with sodium borohydride and on catalytic hydrogenation, deoxyleontalbinine forms a single product which is not identical with allomatridine and sophoridine [7, 10]. From these results, the configuration (I) may be proposed for leontalbinine. Deoxydihydroleontalbinine, a new isomer of matridine, has one of the configurations (II)–(IV). The presence in the IR spectrum of deoxydihydroleontalbinine of the absorption band of a trans-coupled quinolizidine excludes configurations (III) [11].

The structure 11, 12-dehydroisomatridine has been proposed for goebeline [12, 13]. Its IR spectrum has a trans band and the UV spectrum shows absorption at 260 mμ. The reduction of goebeline with lithium aluminum hydride has given deoxytetrahydrogoebeline $C_{15}H_{26}N_2$. It is known that alkaloids containing the grouping $-C{=}C-N-C{=}O$ (aphyllidine, monspessulanine, 5, 17-dehydromatrine, and N-vinylpyrrolidone) have an absorption maxima in the UV spectrum between 240 and 242 mμ and are not reduced by lithium aluminum hydride to a saturated deoxy compound [3, 5, 6, 14], while α, β-unsaturated amide carbonyl groups are reduced with the formation of a mixture of a saturated deoxy base and an unsaturated deoxy base [15].

Moreover, the absorption maxima of the UV spectra of goebeline and sophocarpine, the structure of which has been shown by synthesis, completely coincide [16].

Consequently, the double bond in goebeline is between C_{13} and C_{14}. Since a trans band is found in the IR spectrum of dihydrogoebeline and it differs from matrine, allomatrine, and sophoridine, it must have configuration (V). Thus, configuration (VI) corresponds to goebeline and (IV) to deoxytetrahydrogoebeline. Then configuration (II) remains for deoxydihydroleontalbinine.



Experimental

6.5 kg of L. albertii gathered on the slopes of Galvasai [3] was extracted with chloroform. The concentrated extract was treated with 5% sulfuric acid. This gave a sulfate the base from which had mp 370° C (from toluene) and an IR spectrum coinciding with that of thaspine. The acidic mother solution from the sulfate was made alkaline and the bases were extracted with ether and chloroform. 1.4 g of thaspine, 95 g of combined ether-soluble alkaloids, and 19.2 g of chloroform-soluble alkaloids were obtained, a total of 1.77% of the weight of the dry plant.

From the chloroform fraction of the total alkaloids a hydrochloride with mp 253–255° C (from alcohol) was obtained. The base from it had mp 134–136° C (from petroleum ether). A mixture with N-methylcytisine showed no depression of the melting point.

The ethereal fraction of the total alkaloids (95 g) [R_f 0.23, 0.31, 0.50, 0.68, 0.82, in the isobutanol–concentrated hydrochloric acid–water (50:7.5:13.5) system, M-1 paper, 16–18° C; chromatographing time 18–20 hr; revealing agent Dragendorff's reagent] treated in acetone with an alcoholic solution of hydrogen chloride gave 60.0 g of a crystalline mixture of hydrochloride (R_f 0.68 and 0.82).

The hydrochlorides (60.0 g) were dissolved in 150 ml of water, and an aqueous solution of sodium perchlorate was added. This gave 18.5 g of leontalbine perchlorate with mp 247° C (from alcohol), $[\alpha]_D^{20}$ – 131.2° (c 0.83; alcohol), R_f 0.82.

5 g of the epigeal part of the plant collected in Sidzhak, when treated by the method described above, yielded 1.2 g of thaspine sulfate, 73.2 g of ether-soluble alkaloids and 18.0 g of chloroform-soluble alkaloids; 5.3 g of N-methylcytisine hydrochloride was obtained from the latter. The total combined alkaloids amounted to 1.84% of the weight of the dry plant.

The ethereal fraction of the total alkaloids (73 g) was chromatographed on alumina (1810 g, activity grade II). Elution was carried out with benzene (39.9 g), a mixture of benzene and methanol (24.4 g), methanol (1.7 g), and 5% sulfuric acid.

The benzene fraction (38.0 g) gave leontalbine perchlorate with mp 247° C (from alcohol); the mother liquor from the chloroform extraction gave a perchlorate with mp 245° C (alcohol), R_f 0.80; and 1.7 g of the base from the methanolic eluate gave 1.13 g of albertine with mp 161° C (from acetone), $[\alpha]_D^{21}$ –101.5° (c 2.03; alcohol), R_f 0.35.

Found, %: C 68.50; 68.50; H 8.43; 8.51; N 10.47; 10.52. Calculated for $C_{15}H_{22}N_2O_2$, %: C 68.62; H 8.44; N 10.67; mol. wt. 262.4; mol. wt. 262 (mass spectrometry).

Perchlorate, mp 228–229° C (from alcohol).

Methiodide, mp 285° C [alcohol–acetone (2:1)].

The base obtained from the benzene-methanol fraction (24.3 g) formed a hydrochloride with mp 277–278° C (alcohol–acetone).

Leontalbine. This was obtained from the perchlorate (mp 247° C) in the form of a light-colored oil with bp 180–185° C (5 mm), which darkened in the air, $[\alpha]_D^{26}$ – 167° (c 1.15; alcohol), mol. wt. 246 (mass spectrometry), 22 protons (from the NMR spectrum).

Picrate, mp 214–216° C (from alcohol).

Found, %: C 54.20; 54.00; H 5.64; 5.55; N 14.87; 14.77. Calculated for $C_{15}H_{22}N_2O$. $C_6H_3N_3O_7$, %: C 53.05; H 5.3; N 14.73.

Hydrochloride, mp 275–277° [alcohol–acetone (1:3)].

Found, %: N 9.98; 9.91; Cl 12.66; 12.69. Calculated for $C_{15}H_{22}N_2O$. HCl, %. N 9.37; Cl 11.86.

Methiodide, mp 258–259° C [alcohol–acetone (1:4)].

Deoxyleontalbine. A solution of 1.5 g of the base in 250 ml of absolute ether was treated with 1.2 g of lithium aluminum hydride in 50 ml of absolute ether, and the reaction mixture was heated for 4 hr. Then 15 ml of water was added and it was extracted with ether. The deoxyleontalbine obtained had mp 54–56° C (from ether), R_f 0.43. Yield 1.17 g. IR spectrum: 2800–2700, 1678 cm^{-1}.

Deoxydihydroleontalbine. A solution of 1.0 g of deoxyleontalbine in 30 ml of alcohol was shaken with platinum black (from 0.25 g of PtO_2) in an atmosphere of hydrogen, 100 ml of hydrogen (1.04 mole/mole) being absorbed. The resulting base (0.94 g) formed a hydrochloride with mp 328–330° C (decomp.) [alcohol–acetone (1:2)]. The base from the hydrochloride had mp 60–61° C (from ether) $[\alpha]_D^{25}$ +13.8° (c 1.1; alcohol), R_f 0.51, mol. wt. 234 (mass spectrometry).

Picrate, mp 243–245° C (decomp., alcohol). A mixture with the picrate of *l*-matridine having mp 243–245° C (decomp.) melted at 253–255° C (decomp.).

Found, %: C 47.00; 45.90; H 4.86; 4.75; N 16.08; 15.84. Calculated for $C_{15}H_{26}N_2$. $(C_6H_3N_3O_7)_2$, %: C 46.82; H 4.66; N 16.18.

Hydriodide, mp 306° C (decomp.) [alcohol–acetone (1:2)]. The IR spectrum was identical with that of *l*-matridine hydriodide.

Found, %: I 51.2, 51.1. Calculated for $C_{15}H_{26}N_2 \cdot 2HI$, %: I 52.1.

A mixture of 0.15 g of deoxyleontalbine perchlorate and 0.33 g of sodium borohydride in methanol was heated for 20 min, cooled, and acidified with 5% hydrochloric acid. The residue after the solvent had been distilled off under vacuum was made alkaline with caustic soda and was extracted with methylene chloride. The base formed a picrate identical with that of deoxydihydroleontalbine.

5-Hydroxy-6,7-dehydromatrine. By a published method [11], 3 g of matrine with mp 76° C gave 1.2 g of a base with mp 184–185° C. UV spectrum: λ_{max} 240, 358 mμ (log ε 3.84; 1.8). The IR absorption spectrum agreed with that given in the literature [11].

5-Hydroxymatrine. A solution of 0.95 g of the base (mp 184–185° C) in 30 ml of alcohol was hydrogenated in the presence of 2 g of Raney nickel. The reaction product was chromatographed on 50 g of alumina (activity grade II). Elution with benzene and ether (1:3, 1:4) gave 0.47 g of 5-hydroxymatrine with mp 169–170° C (from acetone). The IR spectrum was identical with that given by Bohlmann et al. [11].

5,17-Dehydromatrine. A mixture of 0.32 g of 5-hydroxymatrine with purified sand and 2 g of phosphorus pentoxide was heated for 5 hr at 160–180° C after which it was treated with ice water, separated from the sand, acidified with 40% caustic soda solution, and extracted with methylene chloride.

The residue after the solvent had been distilled off yielded a perchlorate with mp 244–245° C (from alcohol), $[\alpha]_D^{22}$ +128.3° (c 0.73; alcohol).

Leontalbinine. This was obtained from the perchlorate (mp 245° C) and melted at 107–108° C (from ether), $[\alpha]_D^{24}$ −135.5° (c 0.85; alcohol), R_f 0.80.

Found, %: C 72.60; 72.50; H 9.17; 9.18; N 11.41; 11.48. Calculated for $C_{15}H_{22}N_2O$, %: C 72.09; H 9.00; N 11.37.

Methiodide, mp 295° C [alcohol–acetone (1:11)].

Deoxyleontalbinine. A solution of 1.37 g of leontalbinine in 250 ml of absolute ether was mixed with 1.2 g of lithium aluminum hydride in 50 ml of absolute ether and the mixture was boiled for 10 hr.

After cooling, 10 ml of methanol and 10 ml of water were added and the mixture was extracted with ether. This gave 1.1 g of deoxyleontalbinine R_f 0.37; IR spectrum: 2800–2700, 1670 cm^{-1}.

Hydrogenation of deoxyleontalbinine. 1.0 g of deoxyleontalbinine was hydrogenated over platinum (from 0.405 g of PtO_2) in 20 ml of glacial acetic acid. The solution was made alkaline with 40% caustic soda and extracted with methylene chloride. The deoxydihydroleontalbinine (0.92 g) had mp 65–70° C (from a 1:4 mixture of methylene chloride and absolute ether); R_f 0.50. The main fragments in the mass spectrum of matridine had m/e 219, 205, 176, 163, 151, 137, 123, 111, 100, and 86, and the main fragments in the mass spectrum of deoxydihydroleontalbinine had m/e 234 (M^+), 176, 163, 151, 138, 123, 111, 100, and 86.

Picrate, mp 255–257° C (decomp., from a 2:1 mixture of acetone and alcohol).

Found, %: C 47.70; 47.75; H 4.93; 5.12; N 15.70; 15.96. Calculated for $C_{15}H_{26}N_2(C_6H_3N_3O_7)_2$, %: C 46.82; H 4.66; N 16.18.

Hydrochloride, mp 219–220° C [alcohol–acetone (1:2)].

Hydriodide, mp 357–359° C (decomp., from a 1:5 mixture of alcohol and acetone). The IR spectrum had no absorption bands at 1670–1640 cm^{-1}.

Allomatrine. A solution of 1.66 g of leontalbinine in 30 ml of glacial acetic acid was hydrogenated over platinum (from 0.44 g of PtO_2) at 70–80° C for 22 hr. The solution was concentrated in vacuum, made alkaline with 40% caustic soda solution, and extracted with methylene chloride. The residue yielded a perchlorate with mp 253–254° C (decomp., alcohol). The base from the perchlorate had mp 106–107° C (from ether), $[\alpha]_D^{24}$ +77.4° (c 0.62; alcohol). The IR spectrum coincided completely with that of allomatrine.

Methiodide, mp 297–299° C (decomp., from a 1:3 mixture of alcohol and ether).

Picrate, mp 176–177° C (from acetone).

Deoxydihydroleontalbinine. A solution of 0.10 g of deoxyleontalbinine in methanol was reduced with 0.18 g of sodium borohydride under the conditions of the reduction of deoxyleontalbinine. A picrate with mp 255–257° C (decomp.) identical with that of deoxydihydroleontalbinine was isolated from the reaction products.

Oxidation of leontalbinine. A mixture of 0.42 g of leontalbinine and 0.34 g of chromic anhydride in 20 ml of acetic acid was left at room temperature for 24 hr.

The reaction mixture was diluted with water and extracted with ether. The residue was chromatographed on paper with a reference sample (glutaric acid) in the phenol–water containing 1% of 85% formic acid (3:1) system. The reference sample and the oxidation product gave the same R_f value of 0.68.

Summary

1. The content of combined alkaloids in the epigeal part of Leontice albertii varies from 1.77 to 1.84%.

2. Separation of the combined bases has given thaspine, N-methylcytisine, and the new alkaloids leontalbine, leontalbinine, and albertine.

3. The configuration *l*-5, 17-dehydromatrine has been established for leontalbine and 7, 11-dehydro-15-oxomatridine for leontalbinine.

4. The configuration of 13, 14-dehydro-15-oxo-(5, 6, 7, 11-cis)-isomatridine has been proposed for goebeline.

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