STRUCTURE OF ALBERTRAMINE

B. Sadykov, S. Iskandarov, and S. Yu. Yunusov

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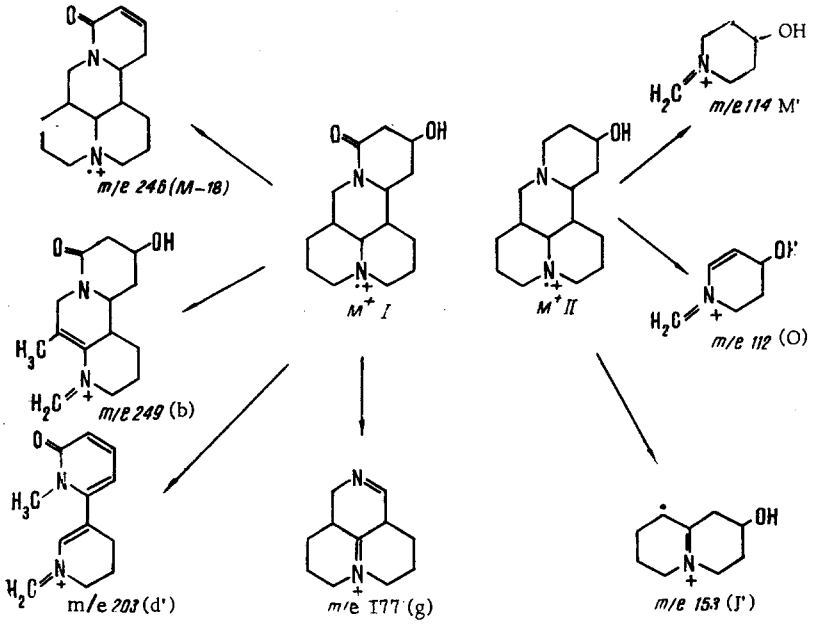
Continuing the separation of the combined alkaloids obtained from the epigeal part of Leontice albertii, we have isolatd a new base with mp 190-192°C, composition $C_{15}H_{24}N_2O_2$, which we have called albertamine. The base possesses monoacid properties and it gives a crystalline perchlorate with mp 119-120°C and a methiodide with mp 248-250°C. The IR spectrum of the alkaloid shows absorption bands indicating the presence in it of a hydroxy group (3300 cm^{-1}) and an amide carbonyl group (1640 cm^{-1}). The UV spectrum resembles the spectrum of dihydroalbertine and has λ_{max} 220 nm [1].

The reduction of albertamine with lithium tetrahydroaluminate formed a saturated hydroxyl-containing base characterized by diacid properties. In the mass spectrum of albertamine (Table 1) as in the spectra of the matrine alkaloids, the peak of $(M-1)^+$ is stronger than M^+. The peak of an ion M−18 has a high intensity. The further pattern of decomposition shows the appearance of peaks of ions as the result of the fragmentation both of the alkaloid and of its anhydro derivative. In actual fact, when albertamine was heated with phosphorus pentoxide anhydroalbertamine was formed, the UV spectrum of which showed the absorption maximum at 263 nm that is characteristic of α,β-unsaturated amides [2]. The mass spectrum of this product showed the peaks of ions that are present in the spectrum of sophocarpine and of 13,14-dehydroisosophoridine [3, 4]. On the basis of a comparison of chemical properties, albertamine can be assigned to the matrine group with a hydroxyl at C_{13} or C_{14}, while the appearance of the characteristic ions can be illustrated by the scheme given below.



The results of the mass-spectrometric analysis have been confirmed by chemical transformations. The dehydration of deoxoalbertamine gave an anhydro derivative in the IR spectrum of which the absorption

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TABLE 1. Main Fragments in the Mass Spectra of Albertamine and its Transformation Products

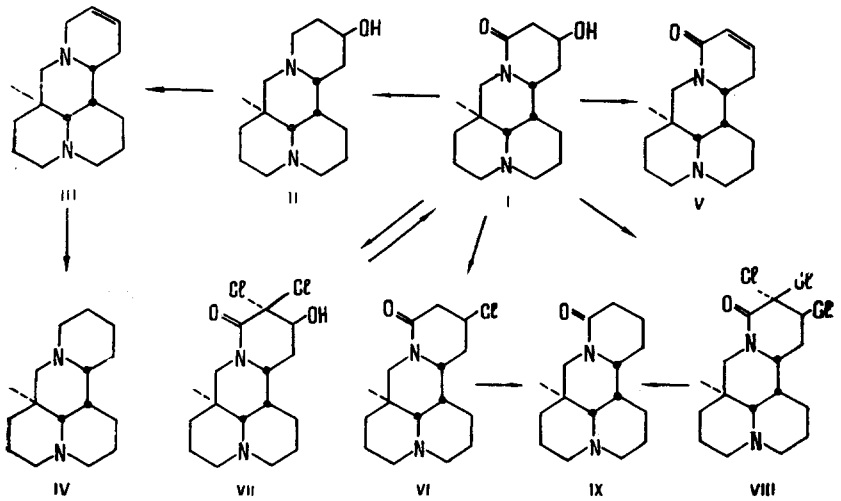
Substance	m/e (relative intensity, %)												
	M^+	a	b	M − 18	c	d	d'	M − (28 + 18)	M − (41 + 18)	e	M − (18 + 56)	f	g
I	264	263	249	246	235	221	203	218	205	192	190	188	177
	(87,0)	(96,5)	(5,3)	(38,0)	(12,1)	(54,3)	(9,3)	(55,5)	(22,6)	(29,9)	(22,6)	(22,2)	(38,7)
II	250	249	235	233	222	207	—	—	—	194	—	192	177
	(100,0)	(38,8)	(4,7)	(13,0)	(10,5)	(17,6)				(9,4)		(13,0)	(15,2)
IV	234	233	219	—	205	191	—	—	—	178	—	176	177
	(100,0)	(39,0)	(1,5)		(8,3)	(18,0)				(3,3)		(12,4)	(15,2)
V	246	245	231	—	217	203	--	—	—	190	—	188	177
	(100,0)	(32,1)	(0,7)		(9,6)	(24,6)				(4,2)		(4,2)	(37,6)

Substance	g'	h	i	i'	j	j'	k	l	l'	m	m'	o	o'
I	193	162	150	—	137	—	122	110	—	98	—	96	—
	(47,5)	(35,0)	(9,2)		(64,0)		(20,6)	(30,8)		(2128)		(100,0)	
II	—	162	150	167	137	153	123	110	126	98	114	96	112
		(42,3)	(30,5)	(18,8)	(17,5)	(9,4)	(16,4)	(18,8)	(11,7)	(82,3)	(16,4)	(70,0)	(30,5)
IV	—	162	150	—	137	—	122	110	—	98	—	96	—
		(29,1)	(77,7)		(87,5)		(15,2)	(14,0)		(55,5)		(59,7)	
V	—	160	150	—	137	—	122	110	—	98	—	96	—
		(15,0)	(79,0)		(30,0)		(36,5)	(34,0)		(50,5)		(56,9)	

band at 3400 cm^{-1} was absent and a band had appeared at 1675 cm^{-1} showing the presence of a double bond. On catalytic hydrogenation, the anhydro derivative formed a saturated oxygen-free compound identical with deoxodarvasamine [5]. Consequently, albertamine is a hydroxy derivative of darvasamine.

When albertamine was chlorinated under various conditions, the replacement of the hydroxyl and of the two hydrogen atoms in the α position with respect to the carbonyl by chlorine took place as in matrine [4], and a trichloro derivative was also obtained. This excludes the presence of the hydroxyl at C_{14}. The catalytic hydrogenation of the dichloro derivative again gave albertamine, and the hydrogenation of monochloroalbertamine and of trichloroalbertamine gave darvasamine [5].

Thus, albertamine has the structure of 13-hydroxydarvasamine.



EXPERIMENTAL

The following solvent systems were used for chromatography: TLC–1) silica gel–gypsum (9:1) with chloroform–methanol (2:1); PC–2) isobutanol–concentrated hydrochloric acid–water (50; 7.5:13.5).

Isolation of Albertamine. The combined alkaloids (180 g) obtained from 10 kg of the epigeal part of Leontice albertii [6] were passed through a column of alumina (diameter of the column 7 cm, 6.2 kg of Al_2O_3). The alkaloids were eluted with benzene, chloroform, methanol, and, finally, a 1% solution of sulfuric acid. The acid aqueous eluate was made alkaline with 25% ammonia solution and the bases were extracted with chloroform. After the solvent had been distilled off, a viscous oil was obtained (1.5 g): R_f 0.4, 0.86, 0.88, 0.90 (system 1).

The mixture of bases was rechromatographed on a column of silica gel. Elution with chloroform gave 10 fractions. Fractions 3-6, after two recrystallizations from acetone, yielded 0.4 g of a base with mp 190-192°C, $[\alpha]_D$ +11.4° (c 0.4; ethanol), R_f 0.86 (system 1), 0.5 (system 2). Perchlorate, mp 119-120°C [ethanol–ether (1:3)]; methiodide, mp 248-250°C (ethanol); picrate, mp 84-85°C (methanol).

Deoxoalbertamine (II). To a solution of 0.2 g of (I) in 300 ml of absolute ether, 0.3 g of $LiAlH_4$ was added in portions, and the mixture was boiled for 4 h. After cooling, the excess of $LiAlH_4$ was decomposed with water and the reaction product was extracted with ether. The residue crystallized on standing, mp 169-170°C (0.1 g), R_f 0.1 (system 1), 0.26 (system 2). The hydrochloride had mp 127-128°C [ethanol–acetone (1:2)].

Anhydro-(II): (III). A mixture of 0.08 g of (II) with purified sand was heated in the presence of 0.5 g of P_2O_5 at 190-210°C for 4 h. The reaction mixture was decomposed with ice and was made alkaline with a 40% solution of caustic potash, and the bases were extracted with ether and then with methylene chloride. Distillation of the ether yielded 0.07 g of a colorless oil, $[\alpha]_D$ −18.6° (c 0.06; ethanol), R_f 0.24 (traces); 0.76 (system 1), 0.63 (system 2).

Dihydro-(III) (IV). A solution of 0.06 g of (III) and the Pt from 0.05 g of PtO_2 in 5 ml of ethanol was shaken in an atmosphere of hydrogen. The amount of hydrogen absorbed was 7 ml (1 mole). The residue consisted of crystals with mp 104-105°C (ether) $[\alpha]_D$ −8.3° (c 0.04; ethanol), R_f 0.24 (system 2).

The hydrochloride had mp 278-280°C [ethanol–acetone (1:1)]. A mixture with deoxodarvasamine hydrochloride gave no depression of the melting point, and the perchlorate melted at 268-269°C decomp., ace-

tone), the methiodide at 318-319°C (ethanol), and the picrate at 184-185°C (decomp., ethanol).

Anhydroalbertamine (V). The heating of 0.15 g of (I) and 0.2 g of P_2O_5 at 190-200°C for 8 h and working up by the method described above gave 0.1 g of a product the separation of which on a thin layer of silica gel yielded substance (V) with mp 136-138°C (ether), $[\alpha]_D$ −83.2° (c 0.02; ethanol), R_f 0.36 (system 1). Hydrochloride, mp 160-162°C [ethanol−ether (1 : 1)].

Monochlorodarvasamine (VI). A solution of 0.05 g of (I) in a mixture of 1 ml each of sulfuryl chloride and thionyl chloride was heated for 30 min. After evaporation of the solvent under vacuum, the residue was dissolved in 5 ml of a 1% solution of hydrochloric acid, this solution was made alkaline with 25% ammonia, and the bases were extracted with ether. The residue (0.04 g) was separated in a thin layer of silica gel. The substance (VI) was isolated in the form of a viscous oil with $[\alpha]_D$ +63.3° (c 0.03; ethanol); R_f 0.84 (system 1), 0.90 (system 2).

Dichloroalbertamine (VII). A solution of 0.05 g of (I) in a mixture of 0.4 ml each of thionyl chloride and sulfuryl chloride was left at room temperature for 15 h. Working up by the method described above gave 0.038 g of reaction product from which the addition of acetone precipitated crystals with mp 144-145°C; R_f 0.90, 0.95 (insignificant) (system 1). The distillation of the solvent from the mother liquor gave the hydrochloride of (VIII) with mp 160-163°C [from ethanol−ether (1 : 2)]; R_f 0.95 (system 1), 0.78 (system 2).

Darvasamine (IX). A mixture of 0.02 g of (VI) and the Pt from 0.04 g of PtO_2 in 5 ml of ethanol was shaken in an atmosphere of hydrogen. The amount of hydrogen absorbed was 2.1 ml (1 mole), and the residue had mp 99-100°C and was identical with (IX). A mixed melting point showed no depression.

Albertamine (I). The hydrogenation of 0.02 g of (VII) over the platinum from 0.01 g of PtO_2 by the method described above gave substance (I) with mp 190-191°C.

CONCLUSIONS

The epigeal part of L. albertii has yielded a new alkaloid, albertamine, which is the 13-hydroxy derivative of darvasamine.

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