SUMMARY

The alkaloids of Datura innoxia cultivated in the Darmi sovkhoz have been studied. As a result, 10 individual bases and two triterpenoids – daturadiol and daturaolone – have been isolated. The amounts of the main alkaloids have been determined. It has been shown that the epigeal part of the plant can also be used for obtaining scopolamine hydrobromide.

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ALKALOIDS OF THE EPIGEAL PART OF Aconitum talassicum. STRUCTURE OF ACTALINE

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The epigeal part of Aconitum talassicum M. Pop. has yielded, in addition to five alkaloids known previously, kobusine, pseudokobusine, and the new alkaloid actaline. The structure of the latter has been established on the basis of an x-ray structural analysis. Actaline is the first C_{20} diterpene alkaloid with a lycoctonine skeleton.

We have investigated the alkaloids of the epigeal part of Aconitum talassicum M. Pop., collected in the flowering phase in the environs of the village of Koksi (Talasskii Ala-Tau range, Kirghiz SSR).

The total amount of alkaloids was 0.7% of the weight of the air-dry plant. By separating the total alkaloids, in addition to the monoacetyltalatisamine, talatisamine, talatisidine, isotalatisidine and talatisine known previously [1, 2], we isolated three other bases.

A base with mp 272-274°C (acetone) had the composition $C_{20}H_{27}NO_2$, $[\alpha]_D$ + 80° (c 1; CH_3OH) and, according to its spectral characteristics, was an alkaloid of the hetisine type. The physicochemical constants and spectral characteristics of the base and its diacetate coincided with those of the alkaloid kobusine. For a definitive identification its methiodide was obtained. A comparison of the crystallographic characteristics of the methiodides of the base and of kobusine showed an identity of the parameters of the elementary cells (with an accuracy of 0.01 Å) and of the space groups, which confirmed the identity of the compounds [3].

The base with mp 268-270°C (acetone) had the composition $C_{20}H_{27}NO_3$. A comparison of spectral and physicochemical constants with literature figures permitted the conclusion that the base was pseudokobusine [4].

The base with mp 125-127°C (hexane) had the composition $C_{22}H_{31}NO_2$ (M 341.23543). Its IR spectrum showed the absorption bands of hydroxy (3475 cm^{-1}) and carbonyl (1680 cm^{-1} groups. The PMR spectrum contained the signals of tertiary C-methyl and N-ethyl groups and a terminal methylene group. In the mass spectrum of the alkaloid, the maximum peak was that of ion M^+ – 15. The base proved to be new and was called actaline. Since the

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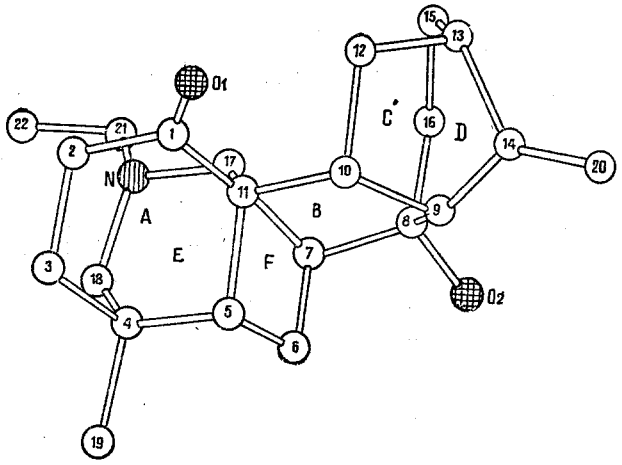


Fig. 1. Spatial structure of actaline.

TABLE 1. Atomic Distances (r, Å) and Valence Angles (ω, deg) in the Structure of Actaline

Distance	r	Angle	ω	Angle	ω
C1—C2	1,47	C2C1C11	119,1	C11C10C12	113,3
C1—C11	1,51	C2C1O1	119,5	C1C11C5	110,8
C1—O1	1,23	C11C1O1	121,1	C1C11C10	103,3
C2—C3	1,55	C1C2C3	111,6	C1C11C17	117,9
C3—C4	1,57	C2C3C4	111,3	C5C11C10	112,9
C4—C5	1,55	C3C4C5	111,9	C5C11C17	99,3
C4—C18	1,55	C3C4C18	109,2	C10C11C17	107,5
C4—C19	1,53	C3C4C19	105,9	C10C12C13	107,3
C5—C6	1,52	C5C4C18	109,3	C12C13C14	101,7
C5—C11	1,53	C5C4C19	112,7	C12C13C15	110,7
C6—C7	1,56	C18C4C19	107,7	C14C13C15	109,5
C7—C8	1,52	C4C5C6	109,2	C9C14C13	104,4
C7—C17	1,56	C4C5C11	108,3	C9C14C20	123,2
C8—C9	1,57	C6C5C11	103,2	C13C14C20	132,5
C8—C16	1,55	C5C6C7	106,8	C13C15C16	113,1
C8—O2	1,43	C6C7C8	110,7	C8C16C15	118,5
C9—C10	1,58	C C7C17	102,9	C7C17C11	99,9
C9—C14	1,50	C C7C17	111,1	C7C17N	115,1
C10—C11	1,53	C7C C9	109,1	C11C17N	111,3
C10—C12	1,55	C7C C16	114,5	C4C18N	113,0
C11—C17	1,55	C7C O2	107,9	C22C21N	110,7
C12—C13	1,54	C9C C16	113,1	C17NC18	112,9
C13—C14	1,50	C9C O2	103,2	C17NC21	108,9
C13—C15	1,57	C16C O2	108,4	C18NC21	113,2
C14—C20	1,35	C9C10C11	115,7	C C9C10	110,9
C15—C16	1,52	C9C10C12	102,9	C C9C14	108,9
C17—N	1,48			C10C9C14	102,5
C18—N	1,49				
C21—C22	1,54				
C21—N	1,50				

alkaloid was isolated in only small amounts, its structure was then shown by the x-ray structural method which demonstrated that actiline has the structure (I).

The spatial structure of the molecule of (I) in projection on the (010) crystallographic axis is shown in Fig. 1. The molecule has a rigid bridge structure consisting of six rings. The cyclohexane ring A (the C1-5 and C11 atoms) has a conformation close to the ideal chair conformation (the C2 and C5 atoms deviate from the plane of the other four by 0.57 and −0.70 Å). The seven-membered ring (the C5-11 atoms) is closer to the boat conformation but is appreciably flattened at C9 (the C5, C6, and C9 atoms deviate from the mean plane of the other four atoms of the ring by 1.29, 1.46, and 0.50 Å, respectively). The five-membered ring C (the C9, C10, and C12-14 atoms) has the form of an envelope with a deviation of the C14 atom from the plane by 0.65 Å. Ring D (the C8, 9, and 13-16 atoms) assumes the form of an unsymmetrically flattened boat (the C14 and C16 atoms deviate by 0.83 and 0.31 Å, respectively). The heterocycle E (the C4, C5, C11, C17, C18, and N atoms) has the form of

TABLE 2. Coordinates ($\times 10^4$) of the Basis Atoms in the Structure of Actaline

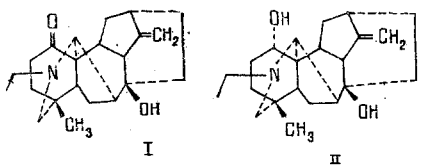
Atom	x	y	z
C1	2317 (14)	1948 (5)	3134 (4)
C2	3090 (15)	1856 (6)	3832 (5)
C3	1341 (17)	1777 (6)	4352 (5)
C4	—274 (14)	1639 (5)	4118 (3)
C5	—1126 (14)	1264 (5)	3474 (4)
C6	—2397 (11)	444 (5)	3157 (4)
C7	—979 (12)	—178 (5)	2714 (3)
C8	—1495 (12)	—73 (5)	1964 (4)
C9	—1687 (13)	994 (5)	1790 (4)
C10	21 (12)	1583 (5)	2125 (4)
C11	676 (12)	1285 (4)	2834 (4)
C12	1797 (15)	1575 (7)	1647 (4)
C13	1085 (16)	1005 (8)	1026 (4)
C14	—1171 (18)	1135 (6)	1057 (4)
C15	1611 (15)	—50 (7)	1118 (4)
C16	—54 (13)	—666 (5)	1477 (4)
C17	1177 (10)	225 (4)	2872 (3)
C18	718 (12)	53 (5)	4109 (3)
C19	—1918 (13)	1037 (5)	4163 (4)
C20	—2556 (15)	1345 (6)	3580 (3)
C21	2755 (15)	—1013 (6)	3439 (5)
C22	4151 (20)	—1385 (7)	4030 (5)
O1	2871 (11)	2625 (4)	2781 (2)
O2	—3553 (7)	—423 (3)	1362 (2)
N	2081 (9)	—94 (4)	3517 (2)

an unsymmetrical chair with the C11 and C18 atoms deviating by 0.89 and —0.57 Å, respectively. The five-membered ring D (the C5-7, C11, and C17 atoms) assumes a distorted half-chair conformation with deviations of the C11 and C17 atoms from the plane of the other three by 0.52 and —0.32 Å. The conformations of the rings and also their linkages in actaline agree with those observed in related diterpene alkaloids with the lycoctonine skeleton — deoxymethylenelycoctonine [5] and delcosine [6] — apart from the conformation of ring A (in them, it has the boat form).

The bond lengths and valence angles are given in Table 1; the errors do not exceed 0.015 Å and 0.8°, respectively. The lengths of the C_{sp^3}—C_{sp^3} bonds range between 1.52 and 1.58 Å, those of the C_{sp^3}—N bonds between 1.48 and 1.50 Å, and those of the C_{sp^3}—C_{sp^2} bonds between 1.47 and 1.51 Å, but within the 3σ limits they may coincide with the corresponding standard values [7]. The lengths of the C=C and C=O bonds are the usual ones.

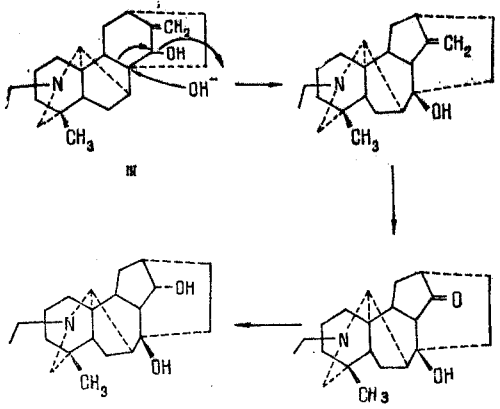
Analysis of the crystal structure of actaline showed the possibility of intermolecular H-bonds of the O(2)—H...O(1) type between the hydroxy and carbonyl groups of the molecules transformed by a 2_1 screw axis [x, 0, 1/4], with a O(2)—H...O(1) intermolecular distance of 1.78 Å and an angle of the A atoms of 162°.

When actaline was reduced with sodium tetrahydroborate, a product (II) was obtained the mass spectrum of which was very close to the spectrum of karakoline and isotalatisidine, in which the peak of the $M^+ - 17$ ion has the maximum intensity in each case, which confirmed that actaline belonged to the diterpene alkaloids of the aconitine type [8] and agreed with the presence in the initial alkaloid of a carbonyl group at C-1. The presence in the mass spectrum of the reduction product of an intense peak of the $M^+ - 56$ ion also agreed with this hypothesis, and that of an intense peak of the $M^+ - 33$ ion with the presence of a hydroxy group at C8. Thus, a $\Delta^{14,20}$-bond has practically no influence on the nature of the mass spectra of the C19 diterpene alkaloids.



I II

Actaline is the first C_{20}-diterpene alkaloid with a lycoctonine skeleton. It is interesting that the lycoctonine alkaloids described in the literature previously had not less than three oxygen substituents. Actaline contains only two oxygen functions and it is undoubtedly of interest from the point of the biosynthesis of the lycoctonine alkaloids, apparently being the first stage of the conversion of the atisine alkaloids [of the type of denudatine (III)] into the lycoctonine alkaloids [9, 10].



EXPERIMENTAL

KSK silica gel and deactivated alumina were used for chromatography.

Mass spectra were recorded on a MKh-1310 instrument with a system for direct introduction into the ion source, IR spectra on a UR-20 spectrometer (KBr), and PMR spectra on a Tesla BS-567 A instrument at 100 MHz.

Isolation of the Total Alkaloids. The air-dry comminuted epigeal part of Aconitum talassicum (31 kg) was wetted with 5% sodium carbonate solution and was then covered with chloroform. The chloroform extract was shaken with 5% sulfuric acid until all the alkaloids had been extracted completely. The sulfuric acid extract was washed with chloroform and was then made alkaline with sodium carbonate and extracted with chloroform. A total of nine extractions was made, and after the elimination of the solvent, 212.5 g of alkaloids were obtained from the chloroform extract and 5 g from the washings.

Separation of the Total Alkaloids. The material from the chloroform extract was dissolved in 5% sulfuric acid. The acid solution was washed with chloroform and was then made alkaline with sodium bicarbonate and extracted first with hexane and then with ether. It was then made alkaline with sodium carbonate and extracted first with ether and then with chloroform. The solvents were distilled off, giving 22.1 g of chloroform washing fraction, 0.01 g of hexane fraction, 5.19 g of ethereal ($NaHCO_3$) fraction (part A), 124.26 g of ethereal (Na_2CO_3) fraction (part B) and 19.65 g of chloroform fraction.

Separation of the Total Alkaloids of Part B of the Ethereal Fraction. When this fraction was evaporated, crystals deposited. The crystals were separated off (2.02 g) and were recrystallized from methanol, and were found to be identical with an authentic sample of talatisine. The residue after the elimination of the ether was treated with acetone, and 26.5 g of technical talatisamine separated out. Part of the mother liquor (2 g) was chromatographed on a column of alumina. Elution was performed in benzene to which methanol was gradually added. Elution with benzene–methanol (50:1) yielded monoacetyltalatisamine (0.02 g) and talatisamine (0.2 g). On elution with the same mixture in a ratio of 25:1, isotalatisidine was isolated (0.28 g). Fractions 27-35 yielded 0.025 g of kobusine. Elution with a mixture in a ratio of 10:1 yielded 0.04 g of talatisidine.

The residue from the acetone mother liquor (66.43 g) was dissolved in 1150 ml of 5% perchloric acid solution. The acid solution was filtered and was washed with chloroform, and was made alkaline successively with sodium bicarbonate, sodium carbonate, and then potassium hydroxide, being extracted with chloroform each time. Fractions I, II, and III were obtained. Fraction I was treated with acetone, and 1.73 g of a crystalline mixture was isolated. This mixture was chromatographed on a column of silica gel (100:1). The column was eluted with chloroform to which methanol was gradually added. On elution with the mixture in a ratio of 100:1, 0.32 g of talatisamine and 0.30 g of talatisidine were isolated.

Fraction II was treated with acetone, which led to the separation of 1.55 g of a crystalline mixture. The crystals were chromatographed on a column of silica gel (150:1). On elution with chloroform–methanol (25:1), 0.03 g of pseudokobusine and 0.55 g of kobusine were isolated.

Separation of Part A of the Ethereal Fraction. When this extract was treated with acetone, 0.20 g of a crystalline precipitate separated out. The mother liquor (4.70 g) was chromatographed on a column of silica gel (100:1). The column was eluted with benzene to which acetone was gradually added and then with acetone to which methanol was added. Elution with benzene–acetone (25:1) yielded 0.20 g of actaline.

Actaline – $C_{22}H_{31}NO_2$ (M 341.23543), mp 125-127°C (hexane.)

Mass spectrum, m/z (%): M^+ 341 (45), 326 (100), 324 (4), 323 (4), 322 (3), 258 (3), 284 (3.5), 267 (26), 266 (2.2), 149 (4.5).

IR spectrum, ν_{max}^{KBr} (cm^{-1}): 3475 (OH), 1680 (CO).

PMR spectrum ($CDCl_3$, δ, ppm, standard - HMDS): 4.51 and 4.53 (1H each, br. s, >C=CH_2), 1.03 (3H, t, >N–C_2H_5), 0.8 (3H, s, $\rangle$C–CH_3), 3.20 (1H, s).

Reduction of Actaline with Sodium Tetrahydroborate. With stirring, sodium tetrahydroborate was added in portions to a solution of 5 mg of actaline in 2 ml of tert-butyl alcohol. The course of the reaction was followed chromatographically. After the end of the reaction, the solvent was evaporated off under suction. The residue was dissolved in water and extracted with chloroform. The chloroform solution was dried over sodium sulfate and evaporated. This gave a chromatographically homogeneous product.

Mass spectra, m/z (%): M^+ 343 (38.5), 328 (41), 326 (100), 287 (45), 284 (15).

X-Ray Structural Analysis of Actaline. The parameters of the cell and the intensities of 1006 reflections ($I \geq 2\sigma$) were measured on a Syntex $P2_1$ diffractometer (CuK_α radiation): a = 6.588(2), b = 14.297(4), c = 19.703(15) Å, d_{calc} = 1.227 g/cm³; space group $P2_1P2_1P2_1$, z = 4. The structure was interpreted by the direct method using the Rentgen-75 program [11] in the automatic regime. Refinement was carried out by full-matrix MLS, first in the isotropic and then in the anisotropic approximation (to R = 0.105). In the last stage of MLS, electron-density difference syntheses were calculated; 23 hydrogen atoms out of the 31 were located. The further refinement of the positions of the basis atoms taking the H atoms found into account, without their refinement, gave a final value of the divergence factor of R = 0.084. The coordinates of the nonhydrogen atoms are given in Table 2.

SUMMARY

The epigeal part of Aconitum talassicum has yielded, in addition to alkaloids isolated previously – monoacetyltalatisamine, talatisamine, talatisidine, isotalatisidine, and talatisine, kobusine, pseudokobusine, and the new base actaline. The spatial structure of the latter has been established by the X-ray structural method.

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