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STRUCTURE OF DICTYSINE

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The results are given of an investigation of the structure of the new diterpene alkaloid dictysine $C_{21}H_{33}NO_3$ isolated from the epigeal part of Delphinium dictyocarpum DC. On the basis of the results of a study of chemical and spectral characteristics, dictysine has been shown to have the sengorine skeleton, with hydroxy groups at C_{15}, C_{16}, and C_{20}.

We have previously reported the isolation from the epigeal part of Delphinium dictyocarpum DC collected in the upper reaches of the R. Koktal in the budding stage of a new alkaloid dictysine [dictyzine] [1].

Dictysine, $C_{21}H_{33}NO_3$ (I), has mp 184-186°C (methanol), $[\alpha]_D^{20}$ −120° (c 1.25; chloroform), mol. wt. 347.2404 [high-resolution mass spectrometry (HRMS)], and it is sparingly soluble in chloroform and readily soluble in acetone and methanol. In the IR spectrum of (I) at 3440 cm^{-1} there is a broad absorption band of hydroxy groups. In the NMR spectrum signals are observed which are due to a tertiary methyl group (0.62 ppm, singlet, 3 H) and an N-methyl group (2.23 ppm, singlet, 3 H). In the mass spectrum of the base there are the peaks of the ions with m/e 347 (M^+, 100%), 330, 316, 312, 304, 256, and 172. Deuteration showed the presence in (I) of three active hydrogen atoms. Consequently, the developed formula of dictysine can be represented as $C_{20}H_{27}(>N{-}CH_3)(OH)_3$.

When (I) was acetylated with acetyl chloride, in addition to the triacetate (II) the diacetates (III) and (IV) were obtained. The empirical and developed formulas of (I), and also the nature of the mass-spectrometric fragmentations of dictysine and the diacetate (III) permit us to assign the base to the diterpene alkaloids of the songorine type [2]. The subsequent investigations confirmed this hypothesis.

A comparison of the mass spectra of dictysine and its deutero analog show that on passing from (I) to its trideutero analog there was a displacement by two mass units of the peaks of the ions with m/e 330 and 316 (Fig. 1a, b), which is connected with the ejection from the molecular ion of OH and CH_2OH groups, respectively. The peak of the ion with m/e 312 did not change, and its appearance is due to the successive ejection of OH and H_2O, as was confirmed by a metastable peak. In addition to those mentioned above, the spectrum of (I) has peaks of ions with m/e 304 and 256. The shift by three mass units of the peak of the first ion in the spectrum of the deutero analog, and also the presence of a metastable peak, showed that this fragment arose through the ejection from the molecular ion of a propyl radical. This was also shown by the HRMS, according to which the ion with m/e 304 corresponded to

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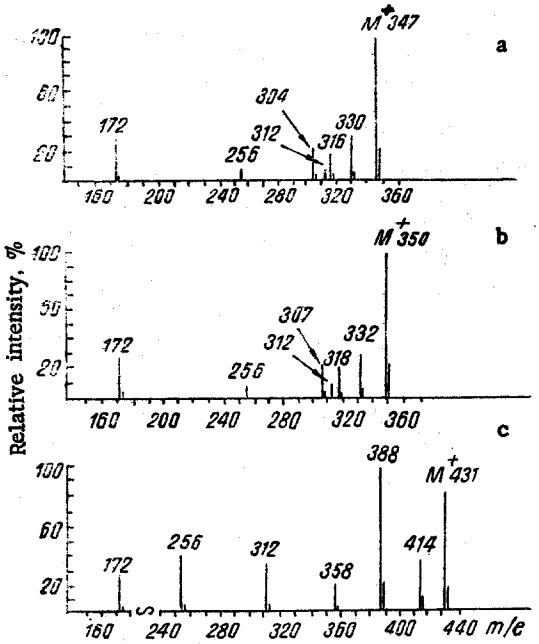


Fig. 1. Mass spectra of dictysine (a), the trideutero analog of dictysine (b), and dictysine diacetate (III) (c).

the composition $C_{18}H_{26}NO_3$. The ion with m/e 256 had the composition $C_{18}H_{26}N$. The presence of a metastable peak showed that it was formed in one stage from the molecular ion by the ejection of a fragment of 91 amu, including all three hydroxy groups, as follows from the spectrum of the deutero analog (I).

What has been stated above permits the conclusion that the hydroxy groups in (I) are located on adjacent carbon atoms and one of them is primary. To confirm this we performed the selective oxidation of (I) with periodic acid. The reaction of dictysine with one mole of periodic acid for three hours gave a compound (V) with M^+ 315. Deuteration showed the presence in (V) of only one active hydrogen atom. Taking this into account, and also the difference in the molecular weights of dictysine and the oxidation product and the presence in the IR spectrum of (V) of a strong absorption band at 1728 cm^{-1}, it may be concluded that oxidation formed a five-membered cyclic ketone. The slightly lowered value of the band of the carbonyl group is apparently due to an α-hydroxy group [3].

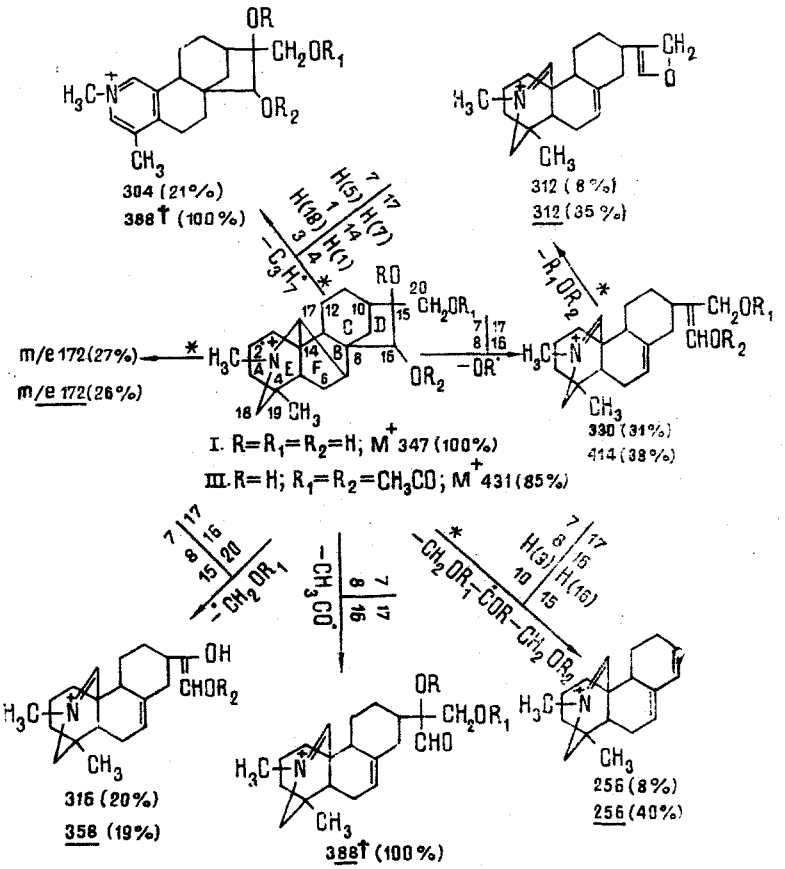
The reaction of dictysine with an excess of periodic acid for three days led to compound (VI) with mp 263-265°C, M^+ 331. In the mass spectrum of (VI), the maximum peak was that of the ion $(M - 29)^+$. The IR spectrum showed a broad absorption band in the 2500-2940 cm^{-1} region and a strong narrow absorption band at 1710 cm^{-1}. The molecular weight of (VI) and also the features of its IR and mass spectra show that oxidation had formed an aldehydo acid. The formation of the latter was confirmed by the NMR spectrum of (VI) in which a one-proton singlet at 9.48 ppm which is characteristic for an aldehyde group appeared.

The formation of compounds (V) and (VI) confirmed the presence in (I) of the songorine skeleton and permitted the hydroxy groups of dictysine to be located in ring D at C_{15}, C_{16}, and C_{20}. The NMR spectrum of dictysine is in harmony with this arrangement of the hydroxy groups in (I); it contains at 3.46 and 4.18 ppm one-proton doublets with J = 12 Hz and at 3.96 ppm a signal in the form of a one-proton singlet. The fact that the one-proton doublets belong to two nonequivalent protons of a C_{20}-methylene group and the one-proton singlet to a proton geminal to the C_{16}-hydroxy group was shown by the disappearance of the first signals in the NMR spectra of (V) and (VI), of the second in the spectrum of (VI) and by the downfield shift of the doublets in the spectra of the acetates (II), (III), and (IV), and of the singlet in the spectra of (II) and (III):

Substance	20 —C— H (ppm) H		16 —C— H (ppm)
Dictysine (I)	3.46	4.18	3.96
The α-hydroxy ketone (V)	—	—	4.13
The aldehydo acid (VI)	—	—	—
The diacetate (III)	4.06	4.31	4.86
The diacetate (IV)	4.17	5.00	3.96
Dictysine triacetate (II)	4.40	4.98	5.12

Thus, on the basis of what has been stated above it is possible to conclude that dictysine has the structure (I) and the α-hydroxy ketone and the aldehydo acids the structures (V) and (VI), respectively.

The proposed structure (I) is confirmed by the ^{13}C NMR spectrum of dictysine, where in the 21.13-86.72 ppm region there are the signals of 21 carbon atoms appearing in the off-resonance spectrum in the form of four singlets, six doublets, nine triplets, and two quadruplets.



Scheme 1. Mass-spectrometric fragmentation of dictysine ‡ and its diacetate (III). The relative intensities of the ions are given in parentheses; the underlined values of m/e are of fragments formed from (III);* metastable transitions recorded for (I);† composite peak; ‡ the elementary compositions of all the dictysine fragments were determined by HRMS.

Structure (I) satisfactorily explains the nature of all the main ions arising in the mass-spectrometric fragmentation of dictysine, which takes place similarly to the fragmentation of songorine and its derivatives [2]. The ions with m/e 330 and 316 are formed after the initial cleavage of the C_7—C_{17} bond through the ejection from the molecular ion of OH and CH_2OH groups, respectively (Scheme 1).

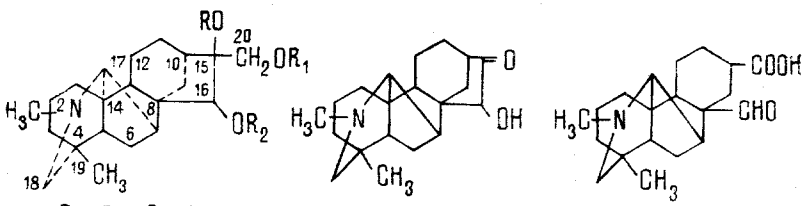
The ions arising after the initial cleavage of the C_7—C_{17} bond also include an ion with m/e 256, which is formed similarly to the M − 58 ion in the case of dihydrosongorine [2], as the result of the ejection from the molecular ion of the elements of ring D. The elimination of the elements of ring A from the molecular ion leads to an ion with m/e 304.

The strong peak of an ion with m/e 172 in the spectrum of (I), which is also present in the spectra of a number of dictysine derivatives, becomes the maximum peak in the spectrum of the α-hydroxy ketone (V). HRMS showed that this ion corresponds to the composition $C_{12}H_{14}N$. Analysis of the spectra of dictysine and of its deutero analog and derivatives permits the conclusion that it is formed as the result of the elimination of the elements of rings A, C, and D from the molecular ion.

So far as concerns the mutual positions of the acetoxy groups in the diacetates (III) and (IV), their presence at C_{15} and C_{20} in the case of (IV) is shown by the fact that on comparing its NMR spectrum with the spectrum of dictysine a downfield shift is observed only of the signals of the C_{20}-methylene group. The downfield shift of the signals of the C_{20}-methylene group and of the signal of the proton at C_{16} in the case of the diacetate (III) (see above) shows that in the latter the acetoxy groups are located at C_{16} and C_{20}. Furthermore, in the mass spectrum of (III) the intensity of the peak of the $(M - 43)^+$ ion rises sharply (Fig. 1c) in comparison with the spectra of (I), (II), and (IV):

Substance	Relative intensity, %					
	M^+	$M-OR$	$M-43$	$M-CH_2(OR_1)$	$M-(CH_2OR_2-C(OR)-CH_2OR_1)$	m/e 172
Dictysine (I)	100	31	21	20	8	27
Dictysine triacetate (II)	15	100	6	—	—	—
The diacetate (III)	85	38	100	19	40	26
The diacetate (IV)	14	20	3	—	—	—

A similar phenomenon has been observed previously for the acetates of songorine, of dihydrosongorine [2], and of napelline [4], which is explained by the ejection of the acetyl radical from the C_{16}-acetoxy group (Scheme 1). In addition to this, in the spectrum of (III) in contrast to the spectra of (II) and (IV) there are the peaks of $(M - 17)^+$ and $(M - 73)^+$ ions arising through the ejection from the molecular ion of the tertiary OH group and a CH_2OCOCH_3 group, similarly to the ejection of OH and CH_2OH groups from the molecular ion in the case of dictysine.



I. $R = R_1 = R_2 = H$
II. $R = R_1 = R_2 = CH_3CO$
III. $R = H$; $R_1 = R_2 = CH_3CO$
IV. $R = R_1 = CH_3CO$; $R_2 = H$

V

VI

EXPERIMENTAL

The homogeneity of the substances was checked by chromatography in thin layers of type KSK silica gel in the benzene—methanol (4:1) and chloroform—methanol (20:1) systems and of "for chromatography" grade alumina in the chloroform—methanol (50:1) system. IR spectra were recorded on a UR-20 instrument in tablets with KBr, NMR spectra in $CDCl_3$ solution on a JMN-4H-100/100 MHz instrument, and the ^{13}C NMR spectrum in Py-D_5 solution on a CFT-20 instrument (in both cases HMDS was used as internal standard and the values are given on the δ scale); low-resolution mass spectra were obtained on a MKh-1303 instrument fitted with a system for direct introduction into the ion source. The deutero analogs of compounds (I) and (V) were obtained by the brief heating of samples in CD_3OD followed by the pumping off of the excess of solvent in the lock system of the mass spectrometer. The elementary com-

positions of the ions were measured on a MS-902 mass spectrometer with a DS-30 data-processing system (United Kingdom).

Acetylation of Dictysine. A solution of 0.3 g of dictysine in 5 ml of acetyl chloride was left in a sealed tube at room temperature for 6 h. The solvent was evaporated off, the residue was dissolved in water, and the solution was made alkaline with cooling and was extracted with ether. The residue after the evaporation of the solvent (0.41 g) was chromatographed on a column of alumina (1:70). The substances were eluted with hexane (18 fractions) and then with hexane–chloroform (100:1), 15-ml fractions being collected.

Fractions 3-17, on treatment with petroleum ether, yielded 70 mg of the diacetate (IV) with mp 131-132°C, fractions 23-28 gave 30 mg of the diacetate (III), and fractions 31-38 gave 64 mg of the triacetate (II).

NMR spectrum of (II): 1.96, 2.03, and 2.1 ppm (3 CH_3COO). Mass spectrum: M^+ 473, 414 (100%), 430, 312.

NMR spectrum of (III): 2.03 and 2.08 ppm (2 CH_3COO). Mass spectrum: M^+ 431, 414, 388 (100%), 358, 312, 256, 172.

NMR spectrum of (IV): 2.00 ppm (2 CH_3COO). Mass spectrum: M^+ 431, 388, 371, 372, 312 (100%).

α-Hydroxy Ketone (V). A mixture of 100 mg of dictysine, 56 mg of periodic acid, and 10 ml of water was left at room temperature for 3 h. Then, with cooling, it was made alkaline with sodium carbonate and was extracted with chloroform. The solvent was evaporated off and the residue (90 mg) was chromatographed on a column of alumina (1:40). The substances were eluted with chloroform and then with chloroform–methanol (10:1). The chloroform eluates yielded 55 mg of (V) and the chloroform–methanol eluates 27 mg of dictysine.

Aldehyde Acid (VI). A mixture of 100 mg of dictysine, 168 mg of periodic acid, and 10 ml of water was left at room temperature for three days. Then, with cooling, it was made alkaline with sodium carbonate, was saturated with ammonium chloride, and was extracted with isoamyl alcohol. The solvent was evaporated off, and the residue was boiled with chloroform. The filtrate obtained after the separation of the part insoluble in chloroform was evaporated, and the residue was treated with acetone to give 50 mg of the aldehydo acid with mp 263-265°C.

SUMMARY

The structure of the new diterpene alkaloid dictysine has been established; it has the songorine skeleton and an α,β,γ-triol system at C_{15}, C_{16}, and C_{20}.

The NMR and mass spectra of dictysine and its derivative have been studied.

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