ALKALOIDS OF *Veratrum lobelianum.*

IX. 15-[(*l*)-2-METHYLBUTYRYL]GERMINE

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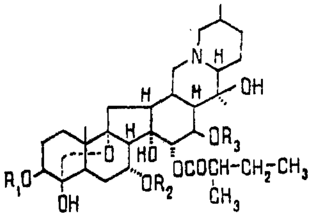
The epigeal part of the plant *Veratrum lobelianum* Bernh., collected in the Caucasus, Alma-Ata province, at the end of the flowering stage, contains 0.48% of a mixture of bases. By separating the ether-extracted fraction of the combined alkaloids on a column of silica gel (eluent chloroform—methanol (9.5 : 0.5)), we have isolated a base with mp 224-226°C (benzene), $[\alpha]_D - 21.48°$ (pyridine), $C_{32}H_{51}NO_9$ (I), M^+ 593. The IR spectrum of the alkaloid contains absorption bands at (cm^{-1}) 3450 (OH), 1735, 1260 (ester C=O). Its PMR spectrum shows singlets at 1.13 ppm (21-CH_3) and 0.89 ppm (19-CH_3), a doublet at 1.02 ppm (CH—CH_3 of the side chain), and a multiplet at 5.26 ppm (C<u>H</u>—O-acyl).

The alkaline hydrolysis of (I) gave an amino alcohol with mp 220-222°C, identical with germine [1] (melting point, IR spectrum) and 2-methylbutyric acid (paper chromatography). The alkaloid (I) proved to be identical in its melting point and IR spectrum with the product of the acid hydrolysis of germerine [2-4], which we have obtained by the action on the latter of methanolic solutions of barium hydroxide (0.05% for an hour) and also of sodium tetrahydroborate (0.4% for 72 h) at room temperature.

The formation of identical products on the partial hydrolysis of germerine shows the splitting out of the acyl group of (*l*-2-methylbutyric acid from C_3 or C_{15} and its location at one of these positions in the alkaloid (I).

For a more accurate determination, the alkaloid (I) was acetylated, giving a triacetyl derivative (II) with mp 250-252°C, M^+ 719, identical with the monoacetyl derivative (IV) of neogermitrine (III), M^+ 719 (melting point, IR spectrum) [5, 6]. Consequently, the (*l*)-2-methylbutyric acid residue in (I) must be located at C_{15}. To confirm this, (I) was subjected to periodate oxidation. This gave an aldehydo-γ-lactone (V) [7], M^+ 591, the IR spectrum of which contained absorption bands at (cm^{-1}) 3450 (OH), 1785 (γ-lactone), 1725 (aldehyde), and 1740 (ester C=O). The IR spectrum of (V) shows the presence of a free OH group at C_3 in the alkaloid (I). Consequently, in (I), the (*l*)-2-methylbutyric acid residue is located at C_{15}.

Thus, the alkaloid (I) has the structure of 15-[(*l*)-2-methylbutyryl]germine, which has been obtained previously by synthesis [8], this being the first time that it has been detected in a plant.



I. $R_1 = R_2 = R_3 = H$ II,IV $R_1 = R_2 = R_3 = COCH_3$
III. $R_1 = R_2 = COCH_3, R_3 = H$

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A STUDY OF THE MECHANISM OF THE INTERACTION OF NUCLEOPEPTIDES WITH DNA BY THE METHOD OF CIRCULAR DICHROISM

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We have previously established that the nucleopeptides L-lysyl-L-β-(thymin-1-yl)-α-alanyl-L-lysine (I) and L-lysyl-L-β-(adenyl-9-yl)-α-alanyl-L-lysine (II) are capable of binding to polynucleotides and causing the stabilization of the double helices of such natural polynucleotides as the DNA of bacteriophage C_D and the double-stranded RNA of bacteriophage f2 [1].

H-L-Lys-X-L-Lys-OH

I. X=L-Tal; II. X=L-Aal; III. X=Gly; IV. X=L-Tyr.

In order to take into account the contribution of electrostatic interactions due to the lysine residues, in parallel experiments we studied the laws of the heat denaturation of complexes of polynucleotides with the nucleopeptides (I) and (II), and also of complexes of the polynucleotides with the reference glycine-containing peptide (III), serving as a standard of comparison.

The experimental results obtained have permitted us to formulate a hypothesis according to which the observed effect of the stabilization polynucleotide helices under the action of nucleopeptides may be due to the formation of hydrogen bonds between the nitrogen bases of the nucleopeptides and the corresponding heterocycles of the polynucleotides. The experimental results available at the present time did not permit definite conclusions to be drawn relative to whether, in this process, the intercalation of the ring systems of the thymine and adenine of the trinucleotides between the nucleic bases of the polynucleotides took place. To solve this problem, we have investigated the circular dichroism (CD) spectra of complexes of DNA with the nucleopeptides (I) and (II) and also with the reference glycine-containing peptide (III) (Fig. 1). It was established that the CD spectra of the polynucleotides scarcely differed in the presence of the nucleopeptides mentioned when recorded in the differential regime relative to the nucleopeptides.

In the light of information obtained previously concerning the laws of change of the CD spectra of complexes of polynucleotides with the tyrosine-containing tripeptide (IV), and also results on the complex-formation of polynucleotides with the peptide antibiotic bacitracin and other ligands [2-4], the new experimental information that has now been obtained on the CD spectra of complexes of DNA with nucleopeptides permits the definite conclusion to be drawn that the ring systems of thymine and adenine present in the structure of nucleopeptides do not intercalate on interaction with DNA but form hydrogen bonds with the hydrogen bases of the DNA, which leads to the stabilization of the DNA double helix.

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