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STRUCTURE OF ACOSEPTINE — A REPRESENTATIVE OF A NEW TYPE OF NORDITERPENOID ALKALOIDS

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A new diterpenoid alkaloid, which has been called acoseptine, has been isolated from the plant Aconitum septentrionale *Koelle. This is the first alkaloid of the anhydrolycoctonine type with a C_8—C_{17} bond and a carbonyl group at C_7. The structure of acoseptine has been established on the basis of IR, mass, and ^1H and ^{13}C NMR spectra.*

The roots of *Aconitum septentrionale* Koelle (*Aconitum lycoctonum*, wolfsbane monkshood) are widely used as a raw material for obtaining lappaconitine — the active principle of the drug allapinin. We have previously [1] reported the isolation from the roots of wolfsbane monkshood of alkaloids accompanying lappaconitine — septerine and septefine. Continuing the investigation of the alkaloid composition of the mother solutions from lappaconitine, we have isolated from wolfsbane monkshood roots a new base with mp 127—128°C, composition $C_{32}H_{44}N_2O_7$, which we have named acoseptine (**1**). Acoseptine is readily soluble in chloroform and less readily in acetone, and it crystallizes from methanol.

The IR spectrum of (**1**) exhibited absorption bands at 3461 and 3354 cm^{-1} (narrow bands, active hydrogen), 1718 cm^{-1} (carbonyl group in a six-membered ring), 1693, 1246, 1098 cm^{-1} (ester group), and 1618, 1591, 760 cm^{-1} (*ortho*-substituted benzene ring). The PMR spectrum of (**1**) contained signals of the protons of a N-ethyl group at 1.00 ppm (3H, t, J = 7.2 Hz), of four methoxy groups at 3.36, 3.37, 3.48, and 3.49 ppm (3H, s, each), and a 19-methylene group at 4.15 and 4.37 ppm (1 H, d, each, J = 11.6 Hz). In the weak-field region of the spectrum there was a broadened singlet at 5.84 ppm (2H, NH_2, disappearing on the addition of CD_3OD) and signals of the protons of an aromatic ring at 6.75 (2H, m, H-3″ and 5″), 7.35 (1H, ddd, ^3J = 8.4 Hz, ^4J = 1.6 Hz, H-4″), and 8.01 ppm (1H, dd, ^3J= 8.4, ^4J = 1.6 Hz, H-6″).

The above information shows that acoseptine is a C-19 norditerpenoid alkaloid containing an anthranilic acid residue at C-18. Moreover, the seven oxygen atoms are components of four methoxy groups, a carbonyl, and an ester group. Consequently, there are no hydroxy groups in acoseptine.

So far as concerns its composition, acoseptine differs by a molecule of water from anthranoyllycoctonine (**2**), which is also present in wolfsbane monkshood roots [2]. As in the case of anthranoyllycoctonine [1], in the PMR spectrum of (**1**) there were signals from H-6α and H-14β in the form of a singlet at 3.93 ppm and a triplet at 3.66 ppm, respectively. In its mass spectrum, the peaks of the M - 15 and M - 31 ions were characterized by considerable intensity [3, 4]. This shows that methoxy group are located at C-1, C-6, and C-14 in acoseptine.

In the ^{13}C NMR spectrum the signals of 32 carbon atoms were observed. It was established by means of a DEPT experiment that, as in the case of anthranoyllycoctonine [5], these signals belonged to five methyl, seven methylene, thirteen methine, and seven proton-free carbon atoms. The assignments of these signals and their characteristics are given in Table 1. The chemical shifts of the majority of the carbon atoms of (**1**) and (**2**) are close, with the exception of the C-6, C-7, C-8, and C-15 atoms of rings *B* and *D*. This shows that acoseptine is an anhydroanthranoyllycoctonine and has the structure (**1**). Such a type of rearrangement as a consequence of which anthranoyllycoctonine undergoes transformation into acoseptine is known in the literature [6]. Substances having an analogous system and a carbonyl group at C-7 are obtained from lycococtonine and

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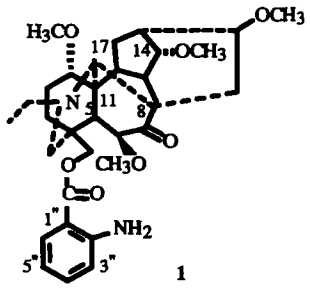
TABLE 1. Chemical Shifts of the Carbon Atoms in the ^{13}C NMR Spectra (1) and Anthranoyllycoctonine (2) in $CDCl_3$

C atom	Multiplicity	1	2	C atom	Multiplicity	1	2
1	d	84.0	84.0	17	d	66.0	64.6
2	t	26.0	26.2	18	t	69.8	68.7
3	t	31.5	32.3	19	t	55.8	52.6
4	s	39.2	37.4	NCH_2	t	42.4	51.0
				|			
5	d	42.4	43.3	CH_3	q	9.9	14.1
6	d	79.4	91.0	1'	q	55.7	55.8
7	s	201.6	88.6	6'	q	59.7	58.6
8	s	59.1	77.6	14'	q	57.0	57.9
9	d	49.1	50.4	16'	q	56.7	53.3
10	d	39.7	38.3	C=O	s	168.1	167.9
11	s	51.4	49.1	1"	s	110.5	110.4
12	t	29.6	28.8	2"	s	150.6	150.9
13	d	46.6	46.2	3"	d	116.6	116.9
14	d	83.4	84.0	4"	d	134.2	134.2
15	t	20.3	33.7	5"	d	116.3	115.4
16	d	83.0	82.6	6"	d	131.2	130.8

other alkaloids with a 7,8-diol system synthetically by their interaction with acetic anhydride and *para*-toluenesulphonic acid [7].

As can be seen from Table 1, singlet signals at 201.6 and 59.1 ppm belong to the C-7 and C-8 carbon atoms. A triplet signal of the C-15 carbon atom is observed at 20.3 ppm. Its upfield shift by 13.4 ppm relative to that of anthranoyllycoctonine is due to the absence of a hydroxy group at C-8.



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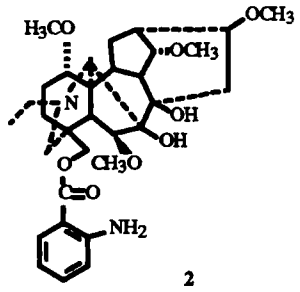

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On the basis of the facts given above, acoseptine is the first alkaloid of norditerpene structure with a new naturally modified type of lycoctonine nucleus.

EXPERIMENTAL

IR spectra were obtained on a Perkin-Elmer System 2000 Fourier IR spectrometer, and ^1H and ^{13}C NMR spectra on a UNITY Plus-400 spectrometer in $CDCl_3$, 0 — TMS. The mass spectrum was taken on a Kratos MS 25 chromato-mass spectrometer (ionizing potential 70 eV, temperature of the source 200°C, temperature of direct injection 120—150°C, collector current 100 μA).

Chromatographic monitoring was effected by TLC (Al_2O_3) in the solvent systems benzene—acetone (1:1) and chloroform—methanol—ammonia (1:1:2 drops).

Isolation of Acoseptine. The mother solution from the total alkaloids of wolfsbane monkshood roots (128 g), after the separation of lappaconitine [2], was dissolved in sulfuric acid, and the solution was washed with ether and fractionally

alkalinized with soda to pH 5, 6, 7, 8, 9, 10, and 12, with extraction by ether at each stage.

The ethereal fractions obtained at pH 7 (24.42 g) and pH 8 (12.62 g) were treated with methanol, and lappaconitine (8.35 g) was separated off and was crystallized from methanol—chloroform (5:1). In this way, 4.01 g of lappaconitine with mp 215—217°C was obtained. The residual crystalline mixture (4.2 g) was chromatographed on alumina with elution by benzene—acetone (1:1) and the collection of 50-ml fractions. On treatment with acetone, the first fraction yielded acoseptine (0.05 g) and the subsequent ones lappaconitine.

Acoseptine, mp 127—128°C (methanol). IR spectrum (KBr, ν, cm^{-1}): 3461, 3354, 2972, 2887, 2818, 2361, 2342, 1718, 1693, 1618, 1591, 1561, 1489, 1457, 1388, 1371, 1341, 1297, 1246, 1209, 1190, 1163, 1120, 1098, 1079, 995, 979, 760.

Mass spectrum, *m/z* (I_{rel}, %) 568 (M^+, 100), 553 (M-15$^+$, 15), 537 (M-31$^+$, 32), 509 (9), 507 (10), 448 (1.5), 419 (4), 406 (6), 375 (8), 374 (27), 346 (7), 281 (3), 256 (4), 219 (3), 218 (9), 187 (6), 185 (30), 150 (6), 149 (35), 121 (16), 120 (64), 92 (22), 91 (30), 83 (34), 71 (58).

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