KARAKANINE – A NEW ALKALOID FROM THE EPIGEAL PART OF Aconitum karakolicum

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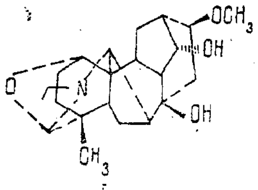
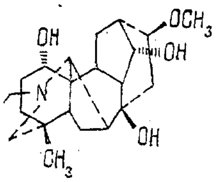
A new alkaloid, which has been called karakanine, has been isolated from the total alkaloids of the epigeal part of Aconitum karakolicum. The structure of karakanine as 8β,14α-dihydroxy-16β-methoxy-4β-methyl-N-ethyl-1α,19α-epoxyaconitane has been proposed on the basis of a study of its IR, PMR, mass, and ^{13}C NMR spectra, and has been confirmed by its conversion into karakoline.

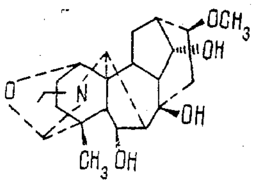
In the course of a further study of the alkaloids from the epigeal part of Aconitum karakolicum Rapaics we have isolated a new alkaloid, which has been called karakanine (I). Karakanine has the composition $C_{22}H_{33}NO_4$. The IR spectrum of the alkaloid had absorption bands of hydroxy groups at 3450 and 3530 cm^{-1} and of ether bonds at 1090 cm^{-1}. The PMR spectrum showed the signals of tertiary C-methyl, N-ethyl, and methoxy groups. In the mass spectrum of the alkaloid the maximum peak was that of the ion $M^+ - 56$, which showed the presence in the alkaloid of an internal α-carbinolamine ether grouping [1]. The Adams reduction of karakanine gave a product that was identified as the alkaloid karakoline (II) [2]. What has been said above permitted the conclusion that the alkaloid was anhydrohydroxykarakoline, which had been obtained previously in the proof of the structure of karakoline. A direct comparison of karakanine with the product of the oxidation of karakoline showed their identity. The proposed structure was confirmed by the ^{13}C NMR spectrum of the alkaloid. The multiplicities of the signals were determined with the aid of the "off-resonance" spectrum. The assignment of the signals was made in comparison with the spectra of karakoline (II) and the alkaloid pentagynine (III), containing an internal α-carboline ether grouping [3, 4]. Consequently, karakanine is 8β,14α-dihydroxy-16β-methoxy-4β-methyl-N-ethyl-1α,19α-expoxyaconitane.



I



II



III

EXPERIMENTAL

For chromatography we used KSK silica gel and deactivated alumina.

Mass spectra were taken 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 and ^{13}C NMR spectra on a Tesla BS-567A instrument at frequencies of 100 and 25.4 MHz, respectively.

Isolation of Total Alkaloids. The air-dry epigeal part of the plant (200 g) gathered in the budding period near Santasha (Kungei Ala-Tau, Kyrgyzstan) was extracted with 80% aqueous ethanol. The ethanol was distilled off, the aqueous residue was cooled, and the precipitate, which did not contain alkaloids, was filtered off. The filtrate was made alkaline with sodium carbonate and was extracted with chloroform. The chloroform extract was evaporated to a volume of 15-20 liters, and the alkaloids were extracted by shaking with 5% sulfuric acid. The acid solution was filtered, and, with cooling, it was made alkaline with sodium carbonate and was extracted with chloroform. Five extractions were made in this way, and, after the solvent had been distilled off, 845 g of total alkaloids (0.42% on the weight of the dry plant) was obtained.

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TABLE 1. Chemical Shifts of Ring Carbons of Karakine (I), Karakoline (II) and Pentagynine (III)

Carbon	II	I	III
1	72,6	91,5	91,2
2	29,1	27,1*	30,2
3	31,5	23,3	23,0
4	33,1	24,4	38,3
5	47,0	37,0	37,3
6	25,4	23,3*	84,3
7	45,4	54,9	56,9
8	74,5	72,3	73,6
9	47,0	45,6**	52,6
10	40,5	38,6	39,0
11	49,1	46,9	47,5
12	29,9	30,5	28,7
13	44,3	45,6**	45,7
14	75,9	75,5	75,5
15	42,5	39,7	39,0
16	82,5	82,0	82,2
17	63,5	61,6	61,7
18	27,8	20,0	20,2
19	60,5	68,9	68,8
N			
CH_2	48,6	48,0	47,8
CH_3	13,3	14,5	14,4
16′	56,6	56,5	56,4

Note. Asterisks denote coinciding carbon atom signals.

Separation of Total Alkaloids. Part of the total alkaloids (45 g) was treated with acetone, and 4.9 g of technical karakoline was separated off. The crystals were recrystallized from acetone, giving 2.1 g of karakoline. The mother liquor from recrystallization was chromatographed on a column of silica gel (ratio of sorbent to substance 100:1) and, after elution with benzene–methanol (80:1), 0.14 g of karakanine was isolated with the aid of acetone.

Karakanine (I), mp 193-195°C (acetone). IR spectrum, ν_{max}^{KBr} (cm^{-1}): 3450, 3530, 1090. PMR spectrum ($CDCl_3$, δ, ppm): 0.80 (3H, s, 4-CH_3), 1.02 (3H, t, N–CH_2–CH_3), 3.29 (3H, s, OCH_3). Mass spectrum m/z (%): M^+ 375(6), 360(4), 346(1), 344(1), 319(100), 304(8), 122(9).

Passage from Karakanine (I) to Karakoline (II). Karakanine (0.03 g) was hydrogenated in 15 ml of methanol over a platinum catalyst for 6 h. After the catalyst had been separated off and the methanol had been eliminated, the residue was dissolved in 2% sulfuric acid. The acid solution was washed twice with ether, and was then made alkaline with sodium carbonate and extracted with ether. The ether was distilled off, and 0.007 g of karakoline was isolated with the aid of acetone.

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