STRUCTURE OF THE NEW ALKALOID SEPTENINE

S. K. Usmanova, V. A. Tel'nov, and N. D. Abdullaev

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A new base – septenine – has been isolated from the roots of Aconitum septentrionale, and its structure has been established on the basis of spectra characteristics.

Continuing the separation of the total alkaloids from wolfsbane monkshood [*Aconitum septentrionale*] [1], we have isolated the known bases N-deacetyllappaconitine, ranaconitine, songorine, lycoctonine, N-deacetylranaconitine, anthraniloyllycoctonine, and septentriosine, and an alkaloid with the composition $C_{22}H_{29}NO_5$, mp 190-192°C, which has proved to be new and has been called septenine (I).

In the IR spectrum of (I) absorption bands were observed from three hydroxy groups at 3570, 3450, and 3345 cm^{-1}, from an ester carbonyl at 1740 cm^{-1} and from a terminal methylene group at ~3080, 1660, and 885 cm^{-1}.

An analysis of the PMR and ^{13}C NMR spectra of septenine together with its elementary composition permitted it to be assigned to the series of C_{20}-diterpene alkaloids. The alkaline hydrolysis of (I) gave the amino alcohol septenidine, $C_{20}H_{27}NO_4$, mp 168-170°C (II).

The IR spectra of (I) and (II) were close to those of acsinatine (III) and septentriosine (IV) [3], which belong among alkaloids of the hetisine type with a C-19 OH group.

The molecular mass of (I) was 16 m.u. greater than that of acsinatine (III), while those of (II) and (IV) were equal (345), but septenidine and septentriosine differed by their physical constants and spectral characteristics.

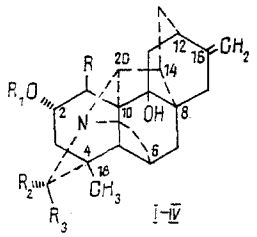
The ^{13}C NMR spectrum of septenine contained the signals of 22 carbon atoms: 6 singlets, 8 doublets, 6 triplets, and 2 quartets.

The assignment of the signals of (I) was made by a comparative analysis with the ^{13}C NMR spectra of acsinatine and septentriosine.

It can be seen from the given details of the ^{13}C NMR spectra of septenine, acsinatine, and septentriosine that the downfield and upfield shifts of the C-4, -18, -19, and -20 signals are due to the orientation of the hydroxy group at C-19.

In the PMR spectra, singlets of the geminal proton (H-19) are seen: in septenine — αH-19 at 4.47 ppm, in acsinatine — αH-19 at 4.51 ppm, and in septentriosine — βH-19 at 4.08 ppm.

These results can be used in determining the orientation of a substituent at C-19.



I–IV

I. R=R₃=OH; R₁=Ac; R₂=H
II. R=R₃=OH; R₁=R₂=H
III. R=R₂=H; R₁=Ac; R₃=OH
IV. R=R₂=OH; R₁=R₃=H

The proposed structure has been confirmed by the two-dimensional PMR spectrum of septenine, which will be published later.

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TABLE 1. Chemical Shifts of the Signals of the Carbon Atoms in the ^{13}C NMR Spectra of Septenine (I), Acsinatine (III), and Septentriosine (IV) [3]

C	I	III	IV	C	I	III	IV
1	67.9	31.8	69.0	13	33.9	34.3	33.1
2	73.1	70.7	70.4	14	43.9	43.9	43.3
3	33.0	37.8	39.1	15	31.1	31.7	30.7
4	42.2	42.2	39.7	16	150.6	152.1	150.3
5	50.8	55.1	58.8	17	104.7	104.3	104.8
6	60.7	60.8	60.5	18	22.2	23.0	28.4
7	30.8	29.6	31.1	19	91.2	92.0	95.2
8	41.7	42.1	42.1	20	67.9	70.1	60.5
9	79.6	78.8	79.8	C=O	170.2	169.6	—
10	53.7	50.4	53.0	|			
11	39.2	39.0	33.5	CH_3	21.6	21.7	—
12	36.2	36.9	36.2				

EXPERIMENTAL

IR spectra were taken on a UR-20 spectrometer; mass spectra on a MKh-1300 mass spectrometer fitted with a system for direct introduction into the ion source; PMR spectra on a BS-567A (Tesla) instrument in $CDCl_3$ with HMDS as internal standard (values given on the δ scale); and ^{13}C NMR spectra on a CFT-20 Varian spectrometer (in $CDCl_3$, 0 — TMDS).

N-Deacetyllappaconitine. The material (32.3 g) of the mother solution after the separation of sepaconitine [1] was chromatographed on deactivated alumina (1:30). Elution was conducted with hexane—ether (1:1), 200-ml fractions being collected. The treatment of fractions 25-31 with a 1:1 mixture of acetone and ether gave a base with mp 208-210°C (0.54 g) which was identified by TLC and by a direct comparison of specimens, and also from its IR and mass spectra, as N-deacetyllappaconitine.

Ranaconitine. The material (31.0 g) of the mother solution from the total wolfsbane monkshood alkaloids after the separation of lappaconitine [1] was chromatographed on a column of alumina (1:40) with elution by hexane and hexane—ether (1:1). Fractions 79-113 (1.53 g) yielded a base with mp 131-133°C (0.58 g) which was identified by an analysis of its spectral (IR, mass, and PMR) characteristics as ranaconitine.

Songorine. The crystalline material (1.31 g) of the mother solution from sepaconitine [1] was washed with benzene. The solvent was distilled off, and the residue was treated with acetone. A base separated out with mp 201-203°C (0.05 g), and this was identified by TLC, by a direct comparison of specimens, and by its IR and mass spectra as songorine.

Septenine. The material (128.0 g) of the mother solution from the total wolfsbane monkshood alkaloids after the separation of lappaconitine [1] was dissolved in 2% sulfuric acid (1300 ml). The acid solution was washed with ether (5 × 300 ml) and was fractionally alkalinized with soda to pH 5, 6, 7, 8, 9, 10, and 12, being extracted with ether (3 × 500 ml) each time.

The ethereal fractions obtained at pH 9 (13.9 g) and 10 (6.49 g) were treated with acetone, and a base was separated off with mp 187-189°C (1.13 and 1.53 g, respectively). The septenine was recrystallized from chloroform—methanol (5:3), mp 190-192°C.

IR spectrum: 3577, 3465, 3345-3080, 1740, 1660, 1445, 1375, 1340, 1287, 1250, 1195, 1170, 1150, 1120, 1080, 1060, 1030, 985, 970, 925, 910, 885, 845, 810 cm^{-1}. Mass spectrum: M^+ 387 (80), 370 (64), 327 (100), 310 (60), 309 (60). PMR spectrum: 1.00 (3H, s, 18-CH_3), 1.99 (3H, s, CH_3CO—), 3.55 (1H, br.s), 4.47 (1H, s, α-H-19), 4.54 and 4.68 (1H each, br.s, 2H-17), 4.95 ppm (1H, br.s, βH-2).

Septenidine. Septenine (0.1 g) was heated in the water bath in 5% aqueous caustic soda for 1.5 h. The solvent was distilled off, and the residue was dissolved in water and extracted with ether, chloroform, and *n*-butanol.

When the butanolic fraction was treated with acetone, (II) separated out, with mp 168-170°C.

Mass spectrum: M^+ 345 (73), 328 (100), 310 (6).

IR spectrum: 3510, 3430, 3160, 1660, 1565, 1550, 1460, 1415, 1350, 1310, 1290, 1250, 1225, 1195, 1173, 1160, 1128, 1080, 1060, 1035, 997, 955, 930, 900, 880, 870, 860, 840, 810 cm^{-1}.

Lycoctonine. The ether fraction (pH 10; 4.71 g) from the mother solution of the total wolfsbane monkshood alkaloids after the separation of lappaconitine was chromatographed on a column of silica gel (1:25). The column was eluted with

hexane—ethyl acetate (1:1), 30-ml fractions being collected. Fractions 20-27 yielded a base with mp 135-137°C (0.12 g) which was identified by TLC and a direct comparison of specimens and by mass spectra as lycoctonine.

N-Deacetylranaconitine. The material (434 g) from the mother solution after the separation of lappaconitine hydrobromide was dissolved in 2.6 liters of 2% sulfuric acid. The acid solution was washed with chloroform (5 × 1.2 liters) and was alkalinized to pH 6, 7, and 10, being extracted with ether (3 × 1.5 liters) each time and finally with chloroform. After the solvent had been distilled off, the ethereal fractions were treated with acetone, which led to the separation of 16.86 g of N-deacetyllappaconitine, and the mother solutions at pH 6 were chromatographed on deactivated alumina (1:60), with elution by benzene and benzene—acetone (50:1), a total of 45 200-ml fractions being collected.

The amorphous base from fractions 42—45 [benzene—acetone (50:1)] was rechromatographed on deactivated alumina (1:50) with elution by ether in 100-ml portions, giving a total of 23 fractions. Fractions 7-9 yielded 0.08 g of a base that was identified by TLC and a direct comparison with a sample of N-deacetylranaconitine obtained from ranaconitine, and also by a comparison of their mass, IR, and ^{1}H NMR spectra.

Anthraniloyllycoctonine. The analogous separation of 366 g of material from the mother solution after the isolation of lappaconitine gave 66 g of a washing chloroform fraction, which was chromatographed on deactivated alumina (1:100) with elution by benzene and the collection of a total of 35 100-ml fractions. Fractions 1—8 (43 g) were rechromatographed on deactivated alumina (1:30), with elution by hexane—ether (5:2 and 1:1) and the collection of a total of 126 120-ml fractions. The treatment with methanol of fractions 36—87 [hexane—ether (5:2 and 1:1)] yielded 3.72 g of a base that was identified by TLC and a mixed melting point with a sample of anthraniloyllycoctonine, and also by a comparison of IR, ^{1}H NMR, and mass spectra.

Septentriosine. The treatment with ether of the mother solution, containing 0.66 g of material, after the separation of septenine, gave 0.39 g of a base, which was identified by its spectral characteristics (mass, IR, and ^{1}H NMR spectra) as septentriosine.

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